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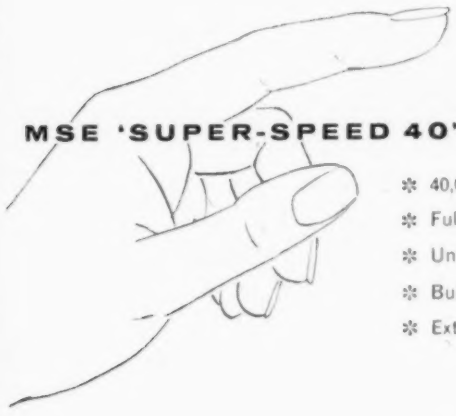

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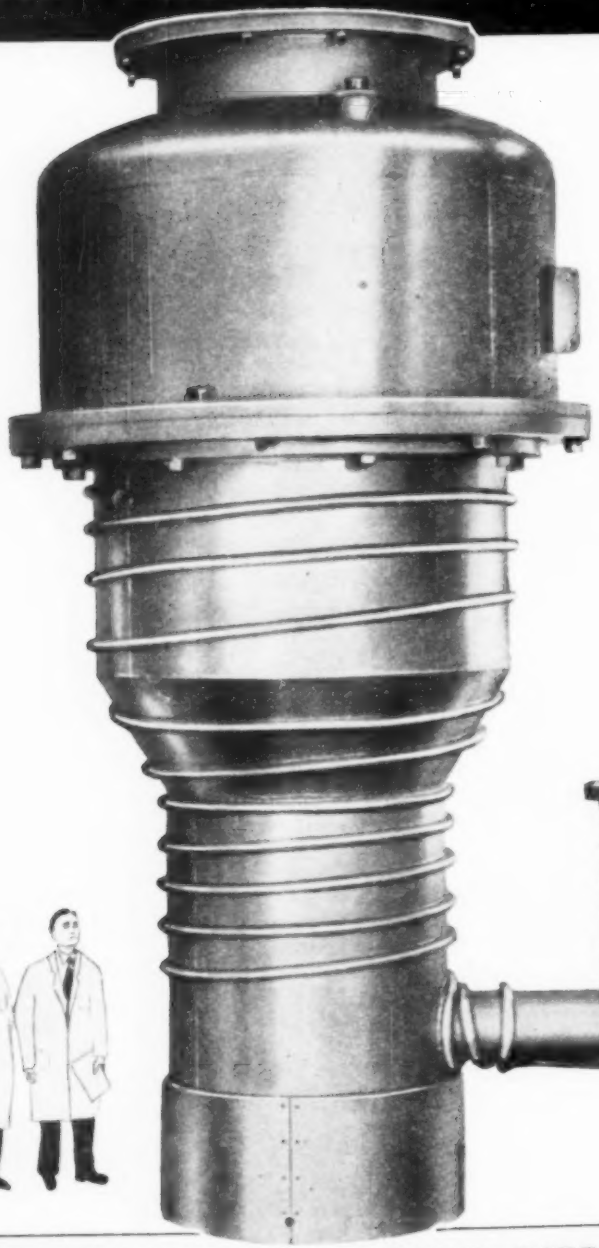

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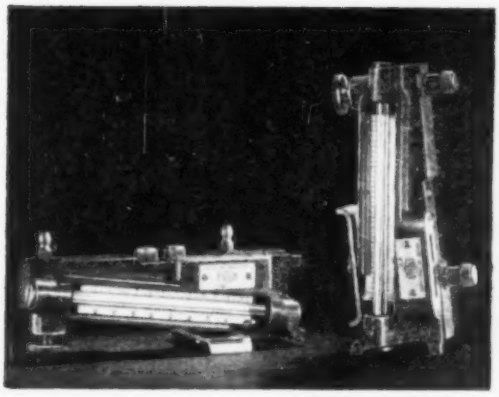

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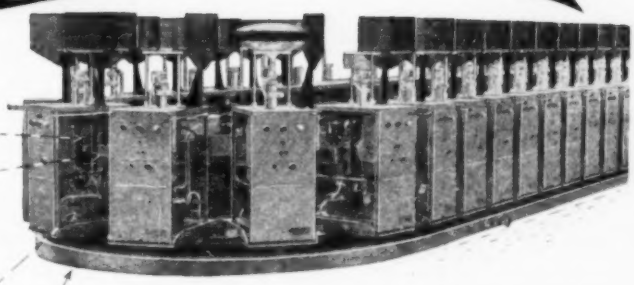

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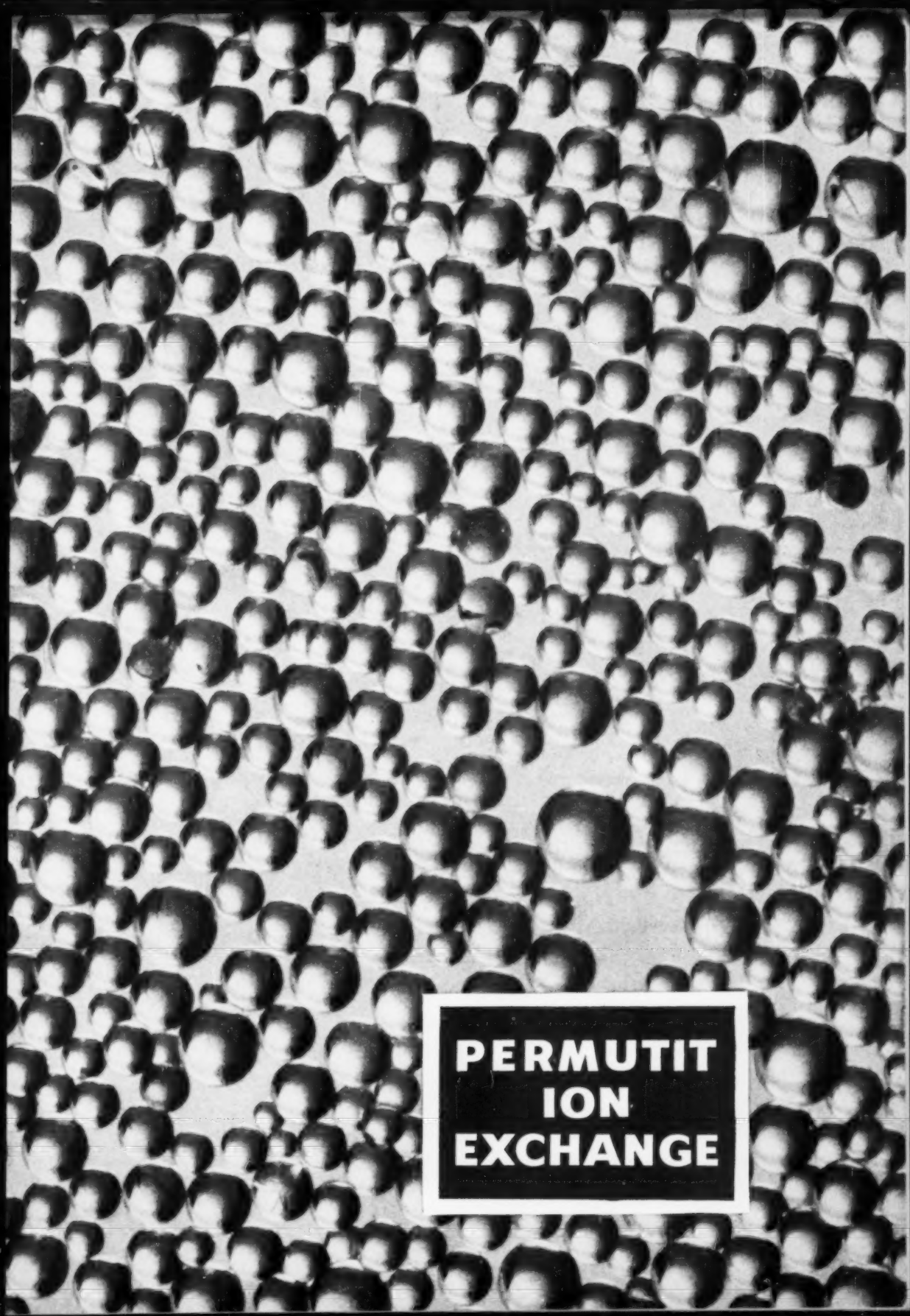
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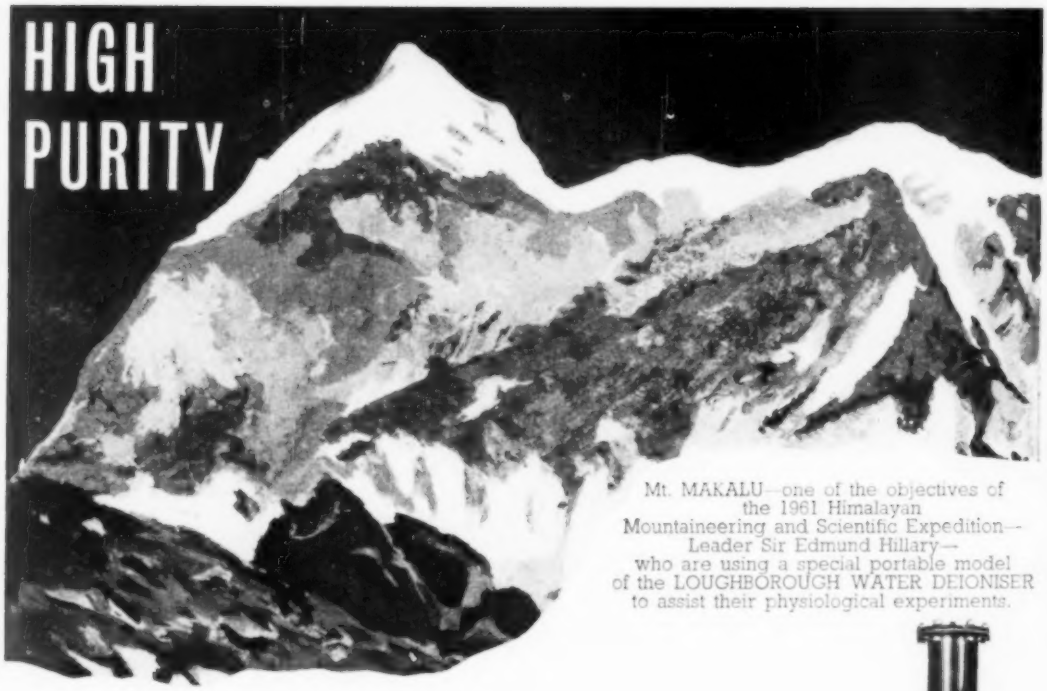

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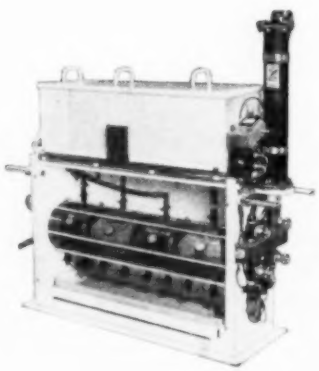

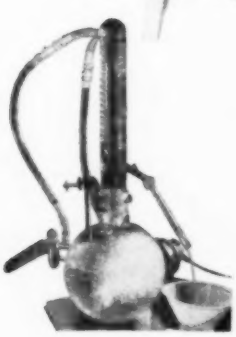

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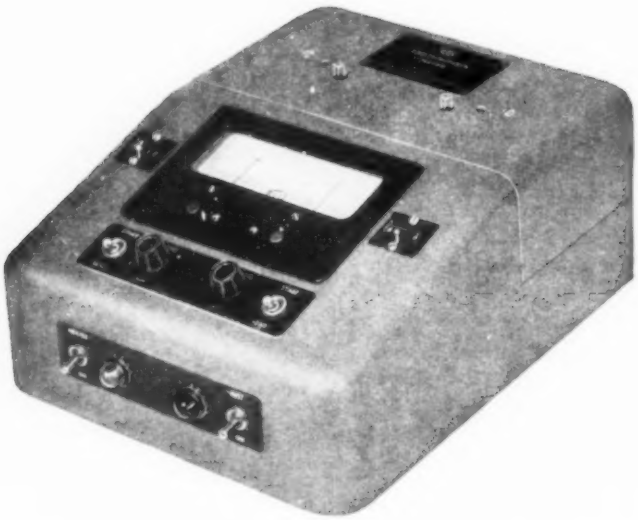

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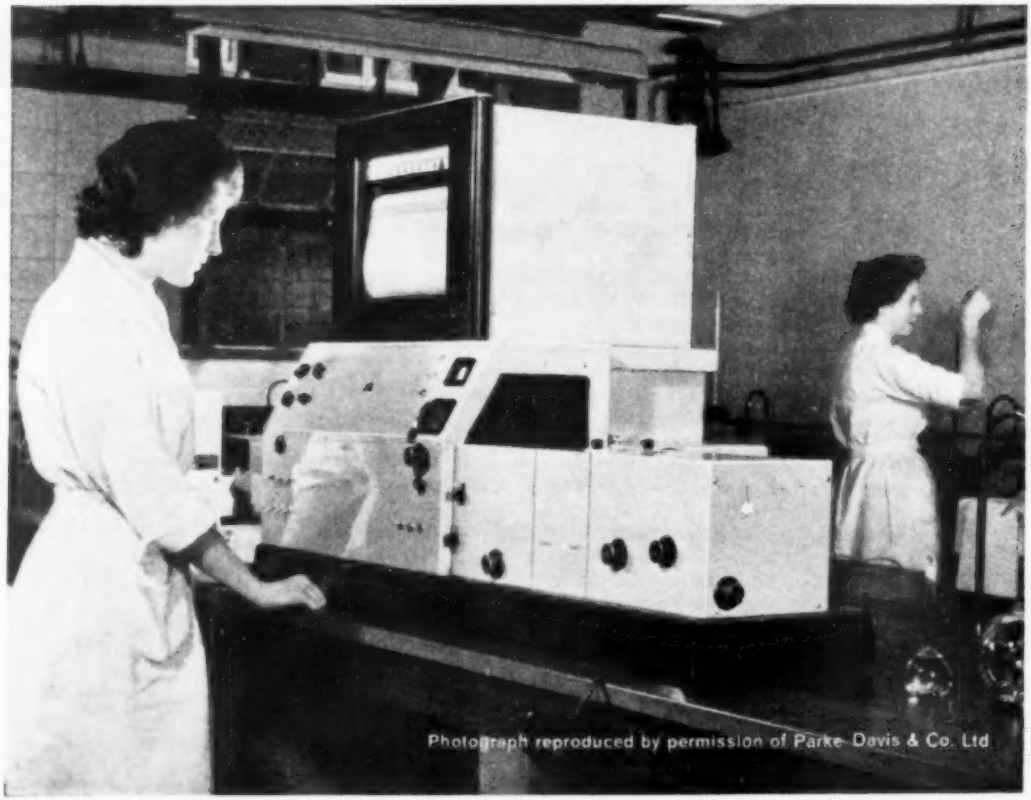

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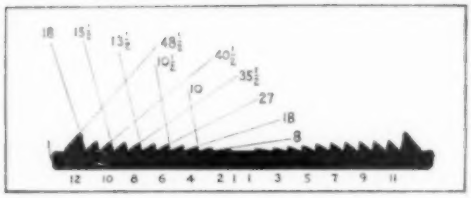

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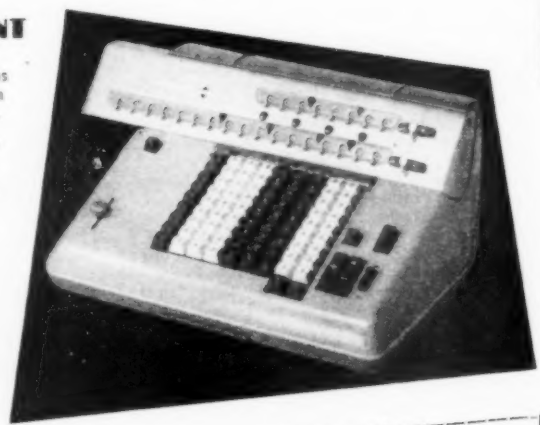

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SCIENTIFIC AND TECHNICAL MAN-POWER IN BRITAIN

IN the recent debate in the House of Commons on the economic situation in Britain, no attention was given to the situation as regards scientific and technical man-power, though this is at least as important as the question of mobility of labour between industry and industry and skill and skill. Nor is it reflected in the report by Political and Economic Planning (see *Nature*, April 15, p. 199), which was so freely quoted in the debate. That report indeed suggests that the chief impediment to a faster growth of the British economy is that we do not want it enough. The British worker is not sufficiently prepared to take risks, to move to a new job and fight for advancement; and in the British business-man also the aggressive, dynamic, restless spirit is less in evidence than the desire for an easy life with safe but small profits.

Political and Economic Planning does not suggest that these natural desires for security should be condemned or ignored; rather they must be faced as valid human needs, which may limit the pace of technological advance and the rate of growth of the economy, but are susceptible to deliberate measures to overcome them. It criticizes the lack of flexibility in industry, and the wasteful hoarding and inefficient use of labour, to which attention was directed in the House of Commons, and it emphasizes the need for Britain to rely on the skill and brain-power of the population to maintain and even improve the standard of living. For that reason alone, social investment, and particularly capital expenditure on education, is regarded as among the most urgent calls on the investment resources of the nation; but in the same connexion, referring to the distribution of public investment, stress is laid on the importance of increasing more rapidly the productivity, and so lowering the cost of coal mining, as well as increasing the efficiency of the railways. Although it is not disputed that heavy taxation does cause some distortion of the economy, and in particular the allowances for depreciation of capital assets are criticized, the PEP study found insufficient evidence to support the more sweeping assertions about the harmfulness of the present taxation system. The allocation of resources, however, is the vital matter, especially where production cannot be immediately increased, and it is admitted that consumption expenditure has not been restrained sufficiently to keep the economy in a healthy condition and to permit a satisfactory steady rate of growth.

One of the reasons for the inadequate rate of growth of the British economy since the Second World War may have been the absence of an objective of growth at which to aim, but PEP can only propose that all efforts should be made by the Government, the employers and the trade unions to increase co-operation in economic life. The rate of growth of productivity could be improved by stepping up the amount of investment; but within this general aim of increasing the level of investment, priority should be given to encouraging labour-saving investments. Attention must also be directed towards increasing the mobility of labour and achieving the maximum flexibility in the labour force; and since the shortage of skilled man-power of all kinds is likely to persist as industry expands, technical education will continue to be a priority and one in which shortage of teachers is likely to be as great a problem as lack of buildings. Apart from this, however, general education at all levels is an important factor in economic progress and the report reiterates that investment in education, apart altogether from its social value, can make a great contribution to production.

What is particularly obvious from the PEP report, without being explicitly stated, is the need for education, scientific research, defence and fiscal policy to be effectively integrated if proper use is to be made of the resources of Britain. It is encouraging to note that there is already some evidence that this is recognized to some extent in the machine-tool industry, where the manufacturers accept that constant work is needed in design, research and development to enable British products to be competitive. The shortage of technically qualified men cannot be overcome by the manufacturers alone; although the industry has provided for scholarships, time will be required before the schools of research and higher training in machine-tool technology now being developed at the Manchester College of Science and Technology, the University of Birmingham, the Royal Technical College, Salford, and the College of Aeronautics, Cranfield, with research grants of more than £100,000 from the Department of Scientific and Industrial Research, or from the special courses at the Birmingham, Loughborough and Salford Colleges of Advanced Technology. Nor can the manufacturers alone solve the problem of improving delivery dates or secure the full benefits of adopting electronic techniques to the control of machine tools without the co-operation of the trade unions.

It is not sufficient, however, for such co-operation and co-ordination to be secured in respect of a single industry. The improved facilities for higher technical education that it needs must form part of a considered policy and programme for expanding technological and technical education in Britain, just as the expansion of its research effort must form part of a considered programme for research and development generally. Further, the demands made for scientific and technological man-power alone interlock the expansion of research and development with that of technological and university education generally.

Obviously many of the necessary decisions have to be taken at the highest possible level. Many of them clearly fall within the sphere of the Minister for Science, but other Ministers are also involved—those of Education, of Power, of Labour, for example, as well as the President of the Board of Trade and the Chancellor of the Exchequer. The ultimate decisions can be taken only at Cabinet-level, but the Minister for Science bears a large responsibility to see that the scientific and technological issues are clearly and forcefully formulated, especially in respect of the demands they make for scientific and technical manpower and provision for its training. The Advisory Council for Scientific Policy, as its last annual report shows, is already clarifying some of the requirements, and the research councils are also examining some of the issues, notably the Council for Scientific and Industrial Research. Some, however, like the Nature Conservancy, appear to lack the resources required even for preparatory exploration, and it should be a first priority on the part of the Minister for Science to see that the task of elucidating all the factors that bear on the distribution of Britain's scientific and technological effort is carried out with the utmost urgency. Only when the results of such a survey are fully available can really sound decisions be taken; in the meantime, it is only too likely that action may have to be taken to strengthen the country's economic position before the full facts are known. The recent debates in Parliament have demonstrated the critical importance of some of the inquiries now being made into particular aspects of Britain's scientific and technological effort, and the urgent need to complete these inquiries at the earliest possible moment.

Mr. Albu, in a recent broadcast talk, suggested that one reason for the backwardness of some sections of British industry is their failure to adapt themselves to the changed educational system and to employ university-trained scientists and engineers not only in research but also in design and production. Possibly Mr. Albu makes too light of the contribution which should also be coming from the colleges of technology, and he may rather over-stress the part that the Government could play in changing the situation. Undoubtedly, however, the Government could ensure that the board of every nationalized industry includes a first-class scientist or technologist, and it could stimulate the backward industries by detailed inquiries such as those made by the Department of Scientific and Industrial Research. It has considerable powers which could be exercised through the research associations, and its authority as a large-scale purchaser could also be used to encourage research. These powers, once again, can only be exercised wisely on the basis of knowledge and not on political theory, and Mr. Albu's suggestions once again really illustrate the decisive position of the Minister for Science and of the Advisory Council for Scientific Policy. On the wisdom and urgency with which Lord Hailsham and his advisers address themselves to these problems depends more than on any other single factor the success of Britain's effort to adjust itself to the world situation of to-day.

THE AGE OF CONFERENCES

Communication or Conflict

Conferences—Their Nature, Dynamics, and Planning. Edited by Mary Capes, with the collaboration of A. T. M. Wilson. Pp. xi + 228 (London: Tavistock Publications, 1960.) 30s. net.

EVERY year, tens, and possibly hundreds, of thousands of people congregate in groups, both large and small, in many different lands. For the most part the purpose of these meetings is the exchange of knowledge and ideas, but some others are held to attempt agreement between delegates whose vital interests may be influenced by any resolutions which may be adopted. Most participants arrive in various conditions of hope and apprehension and depart in varying degrees of despair, stimulation or exhaustion, each with his own opinion of the success or otherwise of the conference.

The book under review is concerned with the factors which make for success or failure. It seems that an "international conference on the functioning of international conferences" was held at Eastbourne during 1956 at some unspecified date, which, from the reference in the foreword to prevailing snow and ice, I can only conclude was within the period January–April. This omission is characteristic of the imprecision of much of the text. The meeting was convened by the World Federation for Mental Health, presided over by Dr. Brock Chisholm (formerly director-general of the World Health Organization) and attended by a mixed bag of social scientists, numbering twenty in all, in which psychiatrists were the most numerous. Three pre-circulated working papers were prepared for the conference entitled: "The Cultural Perspective" (by Margaret Mead), "The Appreciation of Individual Idiosyncrasies" (by Otto Klineberg) and "Historical Development of Group Work" (by T. A. Ratcliffe) and these form Part 1 of the book. Discussion of these papers in plenary sessions led to the setting up of four groups, each having five members who were responsible for leading discussions on a particular topic of the conference. The record of these discussions comprises Part 2. Part 3 consists of four appendixes dealing chiefly with the organization and running of conferences for different purposes.

It is difficult to know what purpose this book will serve. The stated object was "not to provide a rigid set of blue-prints on conference management but to sensitize those interested in small conferences, whether as sponsor or participator, to the subtleties involved when people come together in discussion". Some of the supposed subtleties are so obvious as to be axiomatic, as for example, the cautionary tale on p. 53 of which the moral is to avoid large dormitory accommodation (30 to a room). Some are so masked by verbiage as to be barely discernible, while others are plainly nonsensical. To a physical scientist the notion (p. 14) that "In any conference it is desirable to discount as many as possible of the disadvantages of previous experience or unequal experience—this means that it will be *desirable to equalize language background by having each participant speak in a language not his own*" (my italics) is patently silly.

Scientists are notoriously avid conference goers, and have had to devise semi-empirically sets of rough-and-ready rules appropriate to the successful conduct of their meetings, whether these be large jamborees or small groups of experts discussing

narrow fields, as in the Gordon research conferences, or the informal Faraday Society Discussions, or international delegate conferences charged with specific duties such as agreement on nomenclature or atomic weight standards. The learned societies of Britain and other countries have, among their senior officials, persons with very wide experience of all these types of meetings and of the problems of mechanics, procedure, differences of language and cultural background of the participants, and it is therefore all the more remarkable that apparently not one of these officials was invited to participate in this meeting. One is tempted to think that it would have been difficult for such an official to sit patiently through the "widely exploratory discussion", extending over *three* of the seven days of the meeting, which was apparently necessary before 21 participants could frame the agenda and "draw up an integrated programme of work acceptable to every member". Even then the device of setting up four groups had not been agreed on.

The organizers of international scientific conferences who peruse this book will, despite its many shortcomings, be able to learn some lessons—not all of which may be those intended by the author and contributors. In particular, it is useful to be reminded that each participant arrives with his own characteristic attitudes and preconceptions and his own particular responses towards external problems with which he is presented and which may include a strange language, strange procedures and the establishment of understanding with conference-members of different characteristics and cultural background, and that a prime function of the organizing committee must be to devise machinery which will effectively minimize the barriers which may thereby be created. It might be a salutary exercise for a conference-organizing committee at its first meeting to make a précis of these and related problems and the devices which have been, and might be, adopted to solve them. As a preliminary to this exercise the committee members might, read this book with some profit, though, at the conclusion of their reading, they might well turn to the opening sentence of the foreword in which it is written that the international conference of which this book is the outcome "was perhaps unique" and be forgiven for hoping that it will remain so.

F. S. Dainton

CELLULAR ORGANIZATION

The Organization of Cells and other Organisms
By Laurence Picken. Pp. xxxvii + 629 + 34 plates. (Oxford : Clarendon Press ; London : Oxford University Press, 1960.) 84*s*. net.

THE investigation of the biological cell has received in the past ten years a great impetus, primarily because of the insight that new techniques have given into the structure of its constituent macromolecules. This scholarly book is therefore most opportune, and its relation to present-day trends in cell biology needs careful consideration.

As the author indicates, this is an attempt to integrate the structural aspects of virology, bacteriology and immunology with cytology, and it is the great merit of the book that one author has been able to consider viruses, bacteria, the protozoa and the various structures inside and outside the cells of animals and plants from a single point of view. It must be unique to find an interesting discussion by the same author of, for example, bacteriophage genetics and the cuticle of isopods, and to find an attitude which invites the reader to study not only the observations but also the concepts which inform our attitude to the cell. In this breadth of approach the book compares with the great cytologies of the past and in its emphasis on structure and shape with D'Arcy Thompson's classic work.

There is, however, one major defect, which must be mentioned. This is the refusal, albeit deliberate, to examine, except in general terms, the chemical basis of the fine structures discussed. We thus have the study of macromolecules independently of the molecules which comprise them and with little mention of detailed aspects of their biosynthesis and replication. For example, while Gale's early work on protein synthesis and ribonucleic acid is mentioned, that published by Zamecnik, Hoagland and their colleagues since 1955 is not. A consideration of the latter would surely have modified the sections on cytoplasmic ribonucleic acid, and might perhaps have altered a balance in which three pages are devoted to the endoplasmic reticulum under the heading of "Other Cytoplasmic Membrane Systems", compared with the seventeen pages each devoted to the Golgi apparatus and the mitochondria.

It is also possible to criticize the rather naive template hypothesis of protein synthesis discussed here, and the absence of any mention in this context of possible correlations between base sequence in deoxyribonucleic acid and the composition and structure of proteins. It would also have been most interesting to have had some discussion on the structure of myoglobin in relation to the other protein structures illustrated.

Inevitably, of course, in such a complex book as this, some at least of the interpretations will have been modified even before it reaches the printers. Even so, it is clear that these omissions and others like them arise from the basic philosophy which permeates it, and it is necessary to ask whether it is indeed possible to discuss the organization of cells without a more detailed consideration of their chemistry. Such a requirement might well make an already immense task prohibitive, but there is the alternative of treating a narrower range of biological structures in greater detail. One does not have to hold the extreme view that all biological problems can be solved with the aid of the enteric bacteria and their parasites, to wish that the author had given more time to a discussion of this choice.

This is really the crux of the matter. Imperfect scientists, faced with such a fascinating array of structures, may well be diverted from their immediate problems. May there not be sufficient paradoxes and exceptions in the present narrow fields to stimulate the most lethargic research worker ? Does not the emphasis on the final structure tend to hide an essential unity in ontogeny of everything the cell makes ? It is possible to conceive, and is even probable, that the nematocyst of a coelenterate is synthesized in the same way as the pancreatic enzymes. It may well be that if we knew the contents of one 'black box', we could predict the properties of all the other cellular 'black boxes'.

Whatever our answers to these questions, they can only affect the emphasis that we would put on this or that aspect of structure, and not its

general importance to our understanding of the cell. This careful and well-written account will provide an introduction to a whole range of problems, some of which are in danger of being neglected to-day—an introduction which will be helped by the presence of many plates and diagrams, including a welcome use of X-ray diffraction photographs to illustrate various facets of macromolecular structure. These latter would have been even more valuable, however, if the technique had been briefly described in order that the newcomer might have a better opportunity to appreciate the molecular basis of the identities and differences, which he is asked to see in the illustrations.

The volume with its excellent index and bibliography is, as might be expected, very well produced except for the descriptions which appear under the plates themselves. These are so short as to be misleading in certain cases (for example, Figs. 15·3 and 19·3), and the reader has always to refer to the longer descriptions, collected together at the beginning of the book.

In spite of its shortcomings this is a great personal achievement; in some ways more stimulating because it advances a view of the cell at present unfashionable; if there is one thing to be learnt from this book, it is that fashions change.

P. M. B. Walker

AVIATION METEOROLOGY

Weather Forecasting for Aeronautics

By Joseph J. George. Pp. ix+673. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 15 dollars.

Handbook of Aviation Meteorology

(Air Ministry: Meteorological Office.) Pp. xvi+404+26 plates. (London: H.M. Stationery Office, 1960.) 25*s*. net.

THE first book is fascinating for the meteorologist whether or not he is concerned with the provision of forecasts for aviation. It is essentially a practical manual of techniques and rules for weather forecasting based on a wealth of experience and extensive study over a long period by a man who has for years been concerned with applying meteorology to airline operations.

The results largely apply to the North American continent and are thus not necessarily always directly applicable elsewhere in the world. Nevertheless, the author's techniques and presentation are sure to tempt many forecasters to try the methods out for themselves and will stimulate ideas on how comparable problems might be tackled elsewhere. This is where the book's value to the meteorologist outside North America lies.

It is unique in the field of meteorological literature to come across a book of such practical application that one cannot help but wonder whether meteorological research effort in general is too much devoted to theoretical studies. Perhaps the author himself had this in mind when he says, in reference to other works on the prediction of the movement and development of maritime cyclones, "the material is interesting . . . but it has the drawback of being mostly subjective and providing no numerical answer." This search for a numerical answer is the keynote of the book, with the result that no attempt is made to justify or explain statements and rules in terms of physical and dynamical meteorology. Some of these may cause a raising of eyebrows among the theorists. Mr. George need not make any apology on this score, however, since it is quite apparent that he is dealing throughout with the application of facts emanating from appropriate studies and their justification, and explanation is neither necessary nor appropriate in a book of this nature.

The book can be regarded as composed of three sections. The first (Chapters 2–11) deals with the movement and development of pressure systems and fronts, culminating with two chapters contributed by R. J. Shafer on the computation of pressure changes (referred to as "the Poor Man's Numerical Weather Prediction System") and an example of the construction of a prognostic chart by applying the rules developed in the preceding chapters. Altogether it constitutes nearly half the book and includes practically 100 pages on the movement, deepening and filling of cyclones.

The second covers the prediction of meteorological elements of particular significance to the operation of aircraft, including very low ceilings and fogs, severe weather conditions (thunderstorms, line squalls, turbulence, hail, icing), upper winds and temperatures. It is most comprehensive and includes many useful empirical formulæ. The section is rounded off by a chapter on the use of radar in forecasting.

The third section devotes some 120 pages to local forecast studies relating to 14 airports in the United States. These could well serve as models of the type of work that should be done at every airport in the interest of improving the accuracy and reliability of aerodrome forecasts within the limits of present-day observing practices.

Every forecaster engaged in work for aeronautics should have a copy of Mr. George's book. Although the production is such that it would make a handsome addition to the bookcase, it deserves more than occasional reference and could well justify a constant place on the forecaster's desk as an additional tool for his job. Perhaps it is not too much to hope that it will inspire others to produce similar practical manuals on forecasting for aeronautics in Europe and elsewhere.

Handbook of Aviation Meteorology is a successor to Dr. R. C. Sutcliffe's well known *Meteorology for Aviators* which was first produced in 1938. Dr. Sutcliffe's book has been regarded as the standard text-book, not only in the United Kingdom but also in many other countries, for the meteorological training of pilots and navigators, both civil and military, for their licencing examinations. With the general extension of aviation to higher altitudes and the advancement of meteorological knowledge during the past two decades, there has been an ever-increasing need for a revised version of Dr. Sutcliffe's book. This *Handbook of Aviation Meteorology* will, therefore, be welcomed, particularly by pilots and others concerned with the applications of meteorology to aviation, as fulfilling a long-felt need.

The book includes much new material. It is gratifying to find mention of so many modern operational factors, such as temperature accountability, engine icing, runway visual range, clear air turbulence, helicopter operations, meteorological aspects of aerodrome design, to name but a few, as well as the inclusion of new knowledge about old operational problems, such as thunderstorms and airframe icing.

The treatment of some of the more difficult concepts is particularly good. They are explained lucidly and in detail, with adequate diagrams and illustrations. For example, the 'Tephigram' (so long an imponderable mystery of doubtful purpose to many) will be much more readily understood by the reader of the *Handbook*, and its many uses and value will be better appreciated by the clear examples of its application. Altogether, the evident objective of tailoring the book to suit the reader for whom it is primarily designed is successfully achieved and, in particular, it was a wise decision to keep the mathematics of the derivation of formulæ in an appendix instead of interspersing it in the text.

The only major criticism of this book is that it is already out of date in certain aspects dealing with the procedures for providing meteorological service to pilots and operators. It is recognized that frequent changes occur of necessity in these procedures in order to keep pace with the rapid development of aircraft and airline operations. Nevertheless, for a book published in the jet age of 1960, it is indeed unfortunate that the chapter on "Meteorological Service for Aviation" should largely reflect the position as it was in the first half of the 1950's when so many changes have occurred and new trends emerged since then. It is considered that as this chapter is short (barely 6 pages) it could have been brought up to date immediately before going to press, or could have been written in more general terms to withstand better the weathering of these years of advancement. At the very least the suggestion that for further reading (Appendix 3) one should consult an International Civil Aviation Organization document published in 1951 (and which has been obsolete and out of print for the past five years) should have been corrected.

Fortunately, it is only a very tiny proportion of the whole book that can be criticized in this way. Otherwise it is an excellent production and very well illustrated. It can confidently be predicted that it will be widely used by pilots and other flight-crew members not only as a basic training manual but also as an interesting and readable book of very great value to their work. This book can also be strongly recommended to anyone who wishes to extend his knowledge of meteorology beyond the elementary stage, without scaling the heights of the more advanced text-books on the subject.

THE LITERARY PRESENTATION OF SCIENCE

The Craft of Technical Writing

By Daniel Marder. Pp. xiv+400. (New York and London: The Macmillan Company, New York, 1960.) 35*s*.

HERE we have one more addition to the seemingly endless ranks of books—a large proportion of them coming from America—on how to write scientific and technical, or more properly technological, papers, articles, reviews, reports and even books, including presumably books about how to write scientific and technical, or more properly technological, papers, articles. . . . Is there here not more than a suggestion of the infinite regress?

About two years ago I expressed the opinion (*Nature*, 184, 1749; 1959) that the best of these books, in any event for British writers, was Godfrey and Parr's *The Technical Writer*; I see nothing in the one now before me to justify any revision of the earlier statement. At a rough estimate the earlier book, though 60 pages shorter, contains twice as much useful material, justification for its being 10*s*. dearer than the new one.

Plenty of other books of this class have appeared during the post-War years; one cannot help wondering not only just what they are aiming at but also whether we are to see a continuation of this proliferative growth until every university in the United States, and perhaps every scientific and medical department in the larger ones, will have its own and special manual of presentation, alongside its own text-books of biochemistry, physics, statistical methods, etc.

In the general field of text-books there is such an abundance that the would-be student could not escape complete confusion did not the helpful hand of his professor guide him gently to usage of the proper departmental 'Holy Writ'. No such help is available, however, to the British student faced with a multiplicity of these well-meaning aids to the writing of his own language; he will therefore have to rely on such unintentional warnings as that to be found in Dr. Marder's preface, where he is told that "effective writing comes about through the knowledge and application of rhetorical principles . . ." The mind boggles at the thought of some of our less literary-minded colleagues trying to coat the bitter pill of their writing with the jam of rhetoric.

Admonitions like this destroy the value of much good advice given by Dr. Marder. After all, most rules for writing simple (when simplicity is desirable), clear and unambiguous prose are recognized by him and are indeed the same on both sides of the Atlantic. Nevertheless there are to-day legitimate differences between the two major "English-speaking" countries; a witness to this is the highly significant, even though not generally appreciated, fact that Fowler's seminal *Modern English Usage* has now been replaced by Margaret Nicholson's *A Dictionary of American-English Usage*. This, be it noted, is published in New York by the Oxford University Press, though naturally obtainable in Britain. Fowler's book was published by the same Press, but from Oxford.

Among the many deficiencies of Dr. Marder's book is his complete failure to observe, or even to mention, the invaluable distinction drawn originally by Fowler, and still retained by Nicholson, between the relative pronouns 'which' and 'that'. Again, Dr. Mander must with regret be included in the long ranks of those incurring Prof. A. V. Hill's wrath because they will insist on using 'data' as a synonym for such terms as results, figures or values. Mercifully, though, Dr. Marder has not yet joined the all too rapidly increasing band who cannot recognize the word as a plural noun.

There does not appear to be in this book anything of particular appeal to the British scientific or technological writer. In general, what Dr. Marder advocates is in fact common practice for all those who use the English language with reasonable rectitude in their writing; it differs in no important essentials from the advice to be found in the best post-War books on the subject published (and written) in the United Kingdom. They began, I think, with Kapp's *The Preparation of Technical Information*, now nearly thirteen years old, and they might fittingly be allowed to end, in any event for the present, with

the comprehensive volume by Godfrey and Parr, to which I have already referred. Apart from anything else, legitimate differences in the usage of language between ourselves and our American colleagues naturally receive the American treatment in Dr. Marder's book, which is sufficient to make its use as a guide to British writers a little hazardous, to put it mildly.

There is a felicity of writing that can hardly be taught, but that may perhaps be hardly, in the other sense, acquired, if by no simply definable process; but the ability to handle the English language as an effective tool in the communication of scientific and technical knowledge and information can surely be derived, if at all, from possession and study of Kapp, Gowers, Godfrey and Parr and, perhaps needless to add, Nicholson, since Fowler is no longer with us. I cannot see that Dr. Marder has anything to offer in addition.

A. L. Bacharach

ION TRANSPORT: AN UNORTHODOX VIEW

Transport and Accumulation in Biological Systems
By Dr. E. J. Harris. Second edition. Pp. xi + 279. (London: Butterworths Scientific Publications, 1960.) 50*s*.

THE first edition of Dr. Harris's book appeared eleven years after the War, at the end of a decade in which the use of radioisotopes and flame-photometry had led to a very rapid advance in the knowledge of cell permeability. In the four years which have preceded the publication of a second edition progress has been slower, but a great deal of experimental work has been done, and a digested presentation of this new work is very welcome. The plan of the book remains the same: a few introductory chapters on the physico-chemical features of membrane penetration are followed by accounts of the transport of water, ions, and simple organic molecules by a wide variety of animal membranes; a final chapter gives a brief account of ion movements in plant cells, particularly in giant algal cells and in yeasts. The different animal tissues are described separately, and if this sometimes does less than justice to the resemblances between cells of different types, it discourages that too easy transference of results and hypotheses from one tissue to another, which is a constant temptation to anyone working in this field.

A controversial feature of the book is Dr. Harris's interpretation of equilibration curves. In a number of tissues, including muscle and red cells, the kinetics of ion-exchange between the cell phase and the exterior are not always first order. Dr. Harris explains this by supposing that diffusion in the cell interior is a rate-limiting factor. The more usual explanation is that the departure from first order kinetics comes about because one is dealing with a whole population of cells, differing in size, shape, and probably also in permeability, so that what is observed is the sum of a large number of first order processes. Dr. Harris points out that: "Analysis of kinetics assuming several first order processes is no more than the expression of the first two or more terms of the series describing the diffusion process". This is formally correct, but, though it is good for us to be reminded that the same kinetic behaviour may be predicted by more than one model, it remains true that the population of cells exists, that the cells do vary slightly, and that when the exchange of sodium or potassium in a *single* muscle fibre was examined by Hodgkin and Horowicz, first order kinetics were followed.

The question whether exchange is limited by the membrane resistance or by diffusion in the cell interior is important because it affects one's whole approach to the investigation of ion transport. Consider, for example, the distribution of sodium and potassium across muscle or red-cell membranes. In the conventional view, the chief problem to be solved is the elucidation of the way in which energy from cell metabolism is used to shift ions of a particular species across the cell membrane from a lower to a higher electrochemical potential. In Dr. Harris's view, "There is no reason to expect that metabolic energy is directly involved in the ordinary sodium and potassium turnover processes, for these resemble exchanges on an inert ion exchanger". The need for active metabolism, if the normal intracellular ionic composition is to be maintained, is attributed to the effect of metabolism on the affinity or selectivity of the adsorption sites. If Dr. Harris is right, views on ion transport will have to be completely re-oriented. But, whatever the difficulties of the conventional theory may be, it is not likely that many workers will be as ready as Dr. Harris to dismiss the membrane—at least until there is more evidence for the existence of enough specific adsorption sites within the cell.

I. M. Glynn

LOUIS PASTEUR

Louis Pasteur
A Master of Scientific Enquiry. By Jacques Nicolle. Pp. 196+8 plates. (London: Hutchinson and Co. (Publishers), Ltd., 1961.) 35*s*. net.

JACQUES NICOLLE is well qualified to write about Louis Pasteur. Through family and other connexions he has been able to learn much about the motives and methods of a truly great man whose contribution to science has been far greater than his epoch-making discoveries. This book describes how Pasteur approached and tackled the immediate problem, and, as a result, Nicolle can fairly claim to have produced a great deal more than 'just another biography'.

Louis Pasteur is concerned only with Pasteur the investigator. From his beginnings in stereochemistry to his final essay in human biology, the pertinacious Frenchman approached each investigation in the same way. He never moved until he was steeped in all that was already known; he insisted on examining agronomic and industrial material on the spot; he carried out his researches as near the source of difficulty as possible, even if it meant setting up a makeshift laboratory; he reduced his propositions and his apparatus to the simplest terms; and no tentative claims were made until his results had become self-evident.

In Pasteur's inquiries into the divergent types of tartaric acid, problems of wine- and beer-making, the causes of pébrine and flacherie in silkworms, the nature of anthrax and chicken cholera, the claims of distinguished colleagues to support the truth of abiogenesis (the possibility of which Pasteur never wholly renounced) and the origin of rabies, Nicolle

shows how Pasteur's method of approach never varied and still stands as a model for men of science everywhere. It is indeed a tribute to a man whose father served with Napoleon that his methods are now being applied to the solution of industrial problems. Nicolle's book can take its place as a worthy successor to René Vallery-Radot's admirable *La Vie de Pasteur* and *Les Oeuvres de Pasteur*, which owed so much to its editor, Pasteur Vallery-Radot.

T. H. HAWKINS

TERPENE PROPERTIES AND STRUCTURES

Die Terpene

Sammlung der Spektren und Physikalischen Konstanten. Von J. Pliva, M. Horák, V. Herout und F. Sorm. Teil 1: Sesquiterpene. Pp. xxii + 1–228. (Deutsche Akademie der Wissenschaften zu Berlin: Kommission für Spektroskopie.) (Berlin: Akademie-Verlag, 1960.) n.p.

THIS work is not a compilation of analytical data from all available sources. It is designed not only as an aid to the identification of terpenes but also as material for the study of relations between the infra-red spectra and molecular structure. Advisedly limiting the former objective for the better attainment of the latter, the authors include only physical data determined on the identical sample used for the infra-red work. Largely, therefore, this is a report on a consistent plan of laboratory work, over about twelve years, by a single team at the Czechoslovakian Academy of Sciences.

The plan provides for the fractionation of essential oils, by a standardized technique of distillation followed by alumina-column chromatography, into constituents in which further treatment produces no change of physical characters, including infra-red absorption. These isolates are investigated and classified primarily on the basis of infra-red spectra. Most, though not all, are compounds previously known; but the Prague group has been prominent in the work which in recent years has led to the revision or final elucidation of the structures of such long-known compounds as caryophyllene and humulene (to which, respectively, 9- and 11-membered rings are now assigned), as well as the successful investigation of such new terpenes as the acoran series from calamus oil, embodying spiro-linked 5- and 6-membered rings.

The criterion for classification of a compound is the infra-red spectrum of the saturated hydrocarbon formed by its complete hydrogenation, using Adams's catalyst at room temperature. As a means of investigating structure, it is claimed that this technique, compared with Ruzicka's dehydrogenation procedure, has more general applicability, less risk of altering the carbon skeleton, and has higher yields, permitting of work on smaller quantities. From twenty to thirty carbon skeletons are thus recognized among the sesquiterpenes, and these are named by modification of familiar, or at least identifiable, trivial names, for example, caryophyllan from caryophyllene, zieran from zierone. Sub-groups such as vetivan, isovetivan and neovetivan provide for the *cis-trans* isomerism which may arise naturally or in the course of the hydrogenation.

217 natural or artificial sesquiterpenes are described, each on its own card (British Standard A4 size). A complete card gives molecular and graphic (though not steric) formulæ, density, refractive index and specific rotation, boiling-point (under low pressure) or melting-point, ultra-violet absorption characters if any, a brief indication of source and means of purification, literature references on isolation and constitution, and an infra-red transmittance curve from 650 to 1,500 or 2,000 cm.$^{-1}$, as appropriate, in a rock-salt prism instrument of resolving power 2–3 at 650 and 7–10 at 2,000 cm.$^{-1}$. Experimental data on film thickness, solvent, etc., are supplied.

Indexing, both by classes and by individuals, is adequate. The type correctly indexed as "eremophilan" appears in the structure-key as "eremophyllan".

Further publication on the monoterpenes and higher terpenes, and on the results of gas-chromatographic or other improved methods of separation, is contemplated.

E. G. KELLETT

SERVOMECHANISMS

Control Engineering

(The Van Nostrand Series in Electronics and Communications.) By Prof. Gordon J. Murphy. Pp. xii + 385. (Princeton, N.J.: D. Van Nostrand Company, Inc; London: D. Van Nostrand Company, Ltd., 1959.) 56s.

THIS book presents in some detail the mathematical theory of linear servomechanisms, and, without treating any particular topic exhaustively, describes its application to several different types of system. Techniques for non-linear systems are confined to the two final chapters. So many books have now been published in this field it is probably appropriate to describe in some detail the contents of the present text. After a very general introductory chapter, the second deals with the Laplace transform, the transfer function and related stability considerations under the heading of "Time Response". There follows an excellent chapter on design in the *s*-plane which concludes with a description of the root-locus method. The use of this method is very much a matter of practical experience, but many readers would none the less welcome rather more discussion of its application than is actually included. These two chapters are complemented by the next on frequency response, which covers well-trodden ground in a clear style with several examples to illustrate theory. The three following chapters deal with specific types of system, namely the carrier-control, dead-time and sampled-data systems. A chapter on noise concludes the treatment of linear servomechanisms. The two chapters on the analysis of non-linear systems deal with the describing function and the phase-plane technique.

The text throughout proceeds from the general to the particular, an approach which tends in places somewhat to obscure, or postpone, full appreciation of the significance of a result or technique. The work is therefore not suitable as an introduction to the subject, but forms a useful and clearly written work at a more advanced level.

Problems are included at the end of each chapter, and a table of fifty-two Laplace transforms is included as an appendix.

E. M. DEELEY

Classification and Multiplicity of Growth Layers in the Branches of Trees at the Extreme Lower Forest Border

By Waldo S. Glock, R. A. Studhalter and Sharlene R. Agerter. (Smithsonian Miscellaneous Collections, Vol. 140, No. 1. Publication 4421.) Pp. x + 294 + 36 plates. (Washington, D.C.: Smithsonian Institution, 1960.) n.p.

THIS very detailed study of growth rings in the branches of a number of species of angiosperms and gymnosperms emphasizes the complexity of the problem of the formation of growth rings. The investigation, which was made in Texas, was concerned mainly with trees of the forest border or beyond, where conditions may be assumed to be less favourable for tree growth than within the forest itself. Some of the trees showed multiplicity of growth layers, any one of which might extend over the tree or be confined to a larger or smaller area. One branch, known to be four years old, showed eight growth rings and reference is made to trees subjected to intermittent irrigation which had 15 sharply bordered growth layers formed in four years.

The authors found these growth layers to be extremely varied and sometimes had difficulty in distinguishing between the limits of those formed during a growing season and that which terminated the season. In a distinct seasonal layer it is to be expected that the first-formed cells will be thin walled and perhaps larger than those formed at the end of the increment, where the ring may be well marked by the radial flattening of the last-formed cells or, at least, by a distinct difference between the last-formed cells of the ring and the adjacent first-formed cells of the succeeding ring. No criteria were found by which a false (intraseasonal) ring could be certainly distinguished from one terminating the period of annual growth.

Post-seasonal growth layers were found, that is, incomplete growth-layers produced after the termination of the main seasonal growth, but probably completed before the onset of winter.

Not surprisingly, the authors conclude that ring counts may not be a reliable method of absolute dating and find that frost rings, which could also be induced to form experimentally by the application of dry ice, serve as a more dependable guide.

F. W. JANE

International Review of Neurobiology

Vol. 2. Edited by Carl C. Pfeiffer and John R. Smythies. Pp. xii + 410. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 11 dollars.

THE second volume of *The International Review of Neurobiology*, like the first, is a collection of nine unrelated articles, five of which may be classified as pharmacological. J. Mardones of Chile writes on the addiction of rodents to alcohol; F. W. Schueler of Tulane, on the hemicholiniums; E. J. Walaszek of Kansas, on the cortical pressor-response to epinephrine as affected by schizophrenic serum; E. Costa of Illinois, on serotonin; and A. Herz of Munich, on drugs which influence the conditioned avoidance-response of laboratory-animals. Two articles are mainly biochemical. L. E. and M. R. Hokin of Wisconsin discuss the significance of phosphatidic acid and phospho-inositide in the transport of sodium-ions across neuronal membranes; and E. Roberts and E. Eidelberg of California, the metabolic and neurophysiological roles of γ-amino-butyric acid. The remaining two contributions are both from the United Kingdom. R. M. Gaze of Edinburgh reviews work on the regeneration of the optic nerve in amphibians; and H. J. Eysenck of London describes methods of assessing the value of drugs in cases of psychological illness. All the articles contain much interesting material, but the pharmacological five are less impressive than the other four because of a tendency to build too large a superstructure of assumption on a necessarily slight base of fact. The volume is once again well produced, with full references to the literature and a good index.

DENIS BRINTON

The Observer's Book of Trees

Compiled by W. J. Stokoe. Revised edition. (The Observer's Pocket Series.) Pp. 228 + 12 plates. (London and New York: Frederick Warne and Co., Ltd., 1960.) 5s.

THE Observer's books must be familiar to many. Their size and uniformity make them handy pocket books, and their clarity and arrangement enable easy reference.

This book on trees is a revised edition of that published in 1937. It describes 106 species of the trees and larger shrubs found in the British Isles. Technical terms have been avoided so far as possible, as the aim has been to assist the observer in identification.

There are more than a hundred half-tone photographs, fifty line illustrations and twelve colour plates. These cover the general appearance, bole, foliage, fruit and flower of individual trees, giving excellent impressions at a glance.

One noticeable difference from the original edition is the inclusion of an illustrated guide to 'identification by twigs and buds', which is useful for months when there are no foliage distinctions. Another difference is the newly devised section of coloured plates. These plates, though less beautiful and fewer in number than in the earlier edition, cover far more ground and are of more practical value. Each plate is divided into four or five groups, showing leaf, flower and fruit of fifty-two different trees.

The book has an introduction and two indexes: one classified by families, genera and species; the other alphabetical.

This newly planned edition will be a worth-while purchase for those whose old copies are becoming worn through well-justified use. The price is amazingly low by present-day standards.

B. J. G. MAITLAND

Clays and Clay Minerals

Proceedings of the Seventh National Conference on Clays and Clay Minerals, Washington, D.C., October 20–23, 1958. Edited by Ada Swineford. (International Series of Monographs on Earth Sciences, Vol. 5.) Pp. ix + 369. (London and New York: Pergamon Press, 1960.) 60s. net.

THIS seventh volume continues the excellent tradition of previous volumes. Most of the papers are mineralogical in nature, and constitute useful advances in our knowledge of clay deposits. There is an excellent review article by W. Parrish on the X-ray diffractometer. An article by L. G. Schutz on quantitative X-ray determination of

clay minerals emphasizes the numerous difficulties that still remain in this field. There is a very full study, almost amounting to a monograph, from the Agricultural and Mechanical College of Texas, on the differential settling tendencies of clay minerals in saline waters.

Apart from this article, there are few contributions on the colloidal side of clay mineral studies. However, Dr. R. K. Schofield collaborated in an article on the swelling pressures of sodium montmorillonite pastes, and this must be one of the last contributions he made before his death.

The transference of the publishing of these proceedings from the United States to Great Britain has resulted in a definite deterioration in the standard of binding. But then, few British firms seem able to achieve the quality of binding that is almost uniform in America. They ought to give some attention to the matter. In these times it ought not to require decades for a good technique, possessed by one country, to be transmitted to another.

This volume is edited, with her usual care, by Ada Swineford. I would like to plead with her, however, to have some mercy on bibliographers. These annual proceedings ought to have some short title, by which they can be referred to—I would suggest *Proc. 7th Clay Min. Conf.* The fact that this is Monograph No. 5 of the Earth Science Series seems to be just a blind, designed to make the bibliographical position even more confusing than it already is.

D. M. C. MacEwan

Lowie's Selected Papers in Anthropology

Edited by Dr. Cora du Bois. Pp. xii + 509. (Berkeley and Los Angeles: University of California Press; London: Cambridge University Press, 1960.) 10 dollars; 80*s*.

LOWIE'S memory is well served in this selection of essays by his former pupil and friend Prof. du Bois.

Quite properly, no effort has been made to select material from his eighteen classical monographs on the Plains Indians, or from his ten major books, which ought to stand complete as they are.

Fortunately, Lowie himself had already selected a good deal of material which he regarded as reasonably original and acceptable contributions to anthropological thinking, and in an autobiographical note written in reply to questions from the National Academy of Sciences summarizes his contributions with humility and with the same critical attention that he devoted to all other work.

This selection has been amplified by the editor, who consulted, among others, Kroeber, Radin and Spier. Especially valuable are the six essays left unpublished at his death.

Lowie was completely bilingual in English and German, and fluent in other languages. Moreover, he was thoroughly conversant with the work of great philosophers and scientists, and had all the interests of a well-educated man. About a tenth of his large output was devoted to subjects outside anthropology.

When we read the section on "Theories and Theorists", and note the people whose work he esteemed and critically assessed, we get the measure of the man, and realize why the best anthropologists have come from those who entered the subject with a mind already well developed in other disciplines. In my own view, it is only such people who can give the subject the place it deserves in the universe of discourse among living and civilized minds.

T. K. Penniman

AGARD Aeronautical Multilingual Dictionary

Edited by G. H. Frénot and A. H. Holloway. Pp. xix + 903. (London and New York: Pergamon Press, 1960. Published for and on behalf of Advisory Group for Aeronautical Research and Development, North Atlantic Treaty Organization.) 140*s*. net.

INTERDEPENDENCE between various peoples is particularly pronounced in the aeronautical sciences and well cared for in the Advisory Group for Aeronautical Research and Development under the chairmanship of Th. von Kármán. Thus the Documentation Committee of this Group considered it an important duty to prepare and issue a technical aeronautical dictionary in several languages: Dutch, English, French, German, Italian, Russian, Spanish and Turkish. The first issue is now available and it turns out to be rather more than a dictionary: In fact, it contains translations of the *Glossary of Aeronautical Terms and Definitions* issued by the British Standards Institution (B.S. 185). The translation has been a co-operative effort and has been carried out in each case in countries in which these languages are spoken, except for the translation into Russian, which has been attended to by the British Ministry of Aviation. The result is workmanlike and authoritative, and the *Dictionary* is easy to use. The vocabulary of a rapidly developing science develops with it and it is therefore intended to continue and to expand the dictionary so as to keep it up to date. For this purpose, it is printed on loose punched sheets and supplements can easily be obtained and inserted. In this way, revisions of the source glossary, which is now about ten years old, can also be accommodated. The *Dictionary* is a credit to the editors and their many helpers and it will serve a truly useful purpose all over the world.

D. Küchemann

Wild and Free

Stories of Canadian Animals. By H. Mortimer Batten. Pp. 192. (London and Glasgow: Blackie and Son, Ltd., 1961.) 10*s*. 6*d*. net.

THIS book is a collection of seven stories. Each is about animal adventures, covering such creatures as wolves, deer, beavers, bears, moose, and many others. The stories themselves are both interesting and thrilling, but the book offers something more than this: the reader can learn much about life in the wilds of Canada; and the stories will inculcate a deeper feeling for animals' reactions to environment and circumstance than mere facts can ever portray. It shows that zoology is not merely a text-book subject, but is vivid reality if seen with a sympathizer's eyes.

For example, there is the case of an orphan fawn that makes several attempts, before succeeding, to join a herd of deer when its mother is killed. None of the does will accept it, so from sheer need of companionship, it attaches itself to the buck. From him, by example, it learns how to cope with life at an early age, when the other fawns are still relying on their mothers. Thus it is the only fawn survivor when the herd is attacked by bears.

There are seven full-page illustrations to this, the fifth and last book by the late H. Mortimer Batten.

B. J. G. Maitland

RADIO ASTRONOMY AND COSMOLOGY*

By Prof. MARTIN RYLE, F.R.S.

ASTRONOMY differs from most sciences in that we cannot do experiments; the astronomer must build up from his existing observations a picture or 'model' of the universe, and then look for further effects which should be observable if his model were correct. Although in 700 B.C. the Babylonians were making excellent observations without attempting to interpret them, and although the Greeks proposed models without always looking too carefully into how well they fitted the facts, this approach has always been present, and in the seventeenth century led, through Kepler and Newton, to a good understanding of the solar system.

But what were the stars? Kepler had no conception of their great distance, and imagined them to be on the surface of a fixed sphere with a radius some 2,000 times that of the Earth's orbit. But it seems certain that Newton had a better idea when he wrote:

"But if the matter were evenly disposed throughout an infinite space, some of it would convene into one mass, and some into another, so as to make an infinite number of great masses scattered great distances from one another throughout all that infinite space. And thus might the Sun and fixed stars be formed, supposing the matter were of a lucid nature".

We can see here the first idea of an 'infinite' universe, in which the Sun has no more significance than any of the stars.

There now began the exploration of space on an ever-increasing scale. William Herschel, by constructing larger telescopes than had ever been built before, was able to show that the diffuse band of light of the Milky Way was in fact due to countless stars, and he thus confirmed Newton's suggestion of the insignificance of the Sun. To-day we know that our own Galaxy, the Milky Way system, is a flattened disk containing some 100,000 million stars each comparable in size and luminosity with the Sun.

But the observations of William Herschel and later his son John showed, besides the millions of star images, some thousands of diffuse sources of light or 'nebulæ'. Some of these are now known to be clouds of luminous gas in our Milky Way system, but even at that time the Herschels considered the possibility that these sources were themselves distant 'island universes' too far away for any of the stars to be resolved individually. It was not until methods of distance-measurement had been established in the present century that these suggestions could be confirmed, showing an apparently limitless universe containing, at great separations, compact islands of stars, or galaxies, of which the Milky Way is one.

Besides showing the insignificance of the Earth, these observations raised new problems. One of these, first propounded by the German astronomer Olbers, is based on an observation which any of us can make—that it gets dark at night.

If we look at the sky we see that between the stars it is dark; a larger telescope will see fainter stars here, but again it is dark between them. Now if we must suppose that the universe is infinite in extent, then in whatever direction we look we will eventually see the surface of a star. Although the intensity from each star individually will be very weak, since they must occur in every direction, the sky should have the same brightness as the surface of the Sun: but if this were the case the Earth would be heated to 6,000° and would immediately be vaporized. We cannot avoid the difficulty by supposing that the light from distant stars is absorbed; by the very fact of absorbing the light the obscuring matter will be heated until it has the same temperature as the stars—when it will radiate as much light as it absorbs.

It seems that we can only explain this paradox by supposing that the universe is not infinite. But if we ignore the local stars in our own Milky Way system, we find that the sky is uniformly dark in all directions and we should have to return to a pre-Copernican idea of a universe constructed with us at its centre, having, in the meantime, demonstrated our complete insignificance.

The discovery which eventually led to the solution of the problem was made by the American astronomer Slipher, in 1912. Slipher, who was studying the spectra of the stars in distant galaxies, found that, for a particular galaxy, the spectral lines were displaced slightly, and all occurred on a slightly longer wavelength than expected. This displacement of the lines towards the red end of the spectrum, the so-called 'red shift', is just what would be expected if the light were emitted from a moving source. His observations suggested that not only this galaxy but also a number of others were all moving away from us, and later work led, in 1928, to the conclusion that no matter in what direction one looked, the galaxies were travelling away from us; it was also found that the speed of recession was greatest for the most distant galaxies.

We can now see an explanation for the darkness of the night sky; the light we receive from a very distant galaxy will have suffered such a large red-shift that most of its energy now falls in the infra-red; any visible light received must be emitted in the ultra-violet, where the energy emitted is very small. As a result the light from galaxies beyond a certain distance will be very small, and we have in effect produced a limit to the size of the universe we can see.

Although we have found an explanation for the observations, we have had to introduce the idea of a universe changing with time, and if we relate the rates of recession of galaxies at different distances, we must conclude that all those which we now see must have been crowded close together about 10,000 million years ago. This 'age of the universe' is little more than twice the age of the Earth as indicated by the radioactivity in the oldest rocks. Although the observations cannot indicate whether this period of high density should be regarded as the 'creation' or simply a phase in a universe the density of which varies periodically, they do imply that the appearance of the surrounding universe is changing with time.

In 1948, however, Bondi, Gold and Hoyle proposed an entirely different model, based on the supposition that the universe as a whole is completely unchanging with time. In order to account for the expansion of the universe and the consequent loss to view of

* Substance of a Royal Institution Discourse delivered on February 24.

distant galaxies, they introduced the idea that new matter is continuously created everywhere throughout space; this matter will eventually condense to provide new galaxies to replace those lost to view through the expansion. Although many types of observation and experiment have suggested that matter and energy cannot be created or destroyed, it has never been verified with an accuracy sufficiently high to rule out the theory of 'continuous creation'.

If we accept this Steady-State theory, we have a model which has the philosophical attraction that the universe presents the same appearance no matter from where, or at what time, it is observed. It is a universe unlimited in space or time, and the only unfamiliar feature which we have to accept is that the law of conservation of matter and energy is not quite true.

What we must now ask is whether any of the models proposed bears any resemblance to the actual universe? Here we need to look for subsidiary consequences of the different models and see whether any form the basis for observational test. While it is likely to be very difficult to distinguish between different forms of evolving cosmology, there is a good chance that there are detectable differences between any evolving model and the Steady-State model. In the evolving case we shall expect to find a progressive ageing of the galaxies, and the average distance between galaxies will steadily increase; on the Steady-State model new galaxies are being born to replace those lost by the expansion and we shall always find a mixture of old and young galaxies in any sample we choose.

If, therefore, we could compare a photograph of the surrounding galaxies taken a thousand million years ago with one taken to-day, we should be able to make this distinction. Although this particular experiment is impossible, we can do something very like it by observing galaxies at a distance of a thousand million light years. What we see is a picture of these galaxies as they were when the light left them, and since the light has been travelling for a thousand million years, we can see what changes have occurred in this time by comparing them with nearby galaxies, from which the light has taken a much shorter time to reach us. By extending our observations to greater and greater distances we can in this way explore back to earlier and earlier periods in the history of the universe. This is the reason why astronomers want to study the faintest galaxies, and why the great 200-in. telescope on Mount Palomar was built. Unfortunately, even with this telescope, it has so far proved impossible to reach any definite conclusion, owing to the difficulties of making sufficiently accurate observations of sufficiently distant galaxies.

There seemed little hope of overcoming a barrier apparently so serious; but in 1952 a most remarkable discovery was made—that the second most intense source of radio waves which had been detected in the new science of radio astronomy was a very distant galaxy, at a distance of 500 million light years. Its intensity showed that its radio emission was about a million times more powerful than that of our own or other nearby galaxies.

The fact that a source of such power could exist was surprising enough, but almost as remarkable was the evident rarity of such sources; there are about 100 million galaxies within a distance of 500 million light years, and yet only this one produces radio emission so intense.

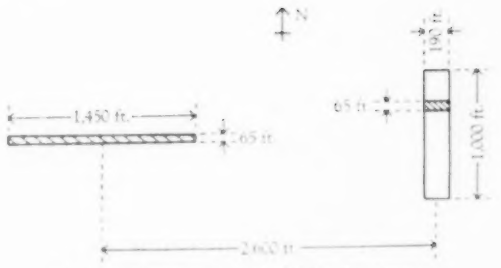

Fig. 1. Diagram of the Cambridge interferometer

More detailed observations with the 200-in. telescope at Mount Palomar suggested that this source was a collision between two complete galaxies. This explained the rarity of such sources (for the chance of such an encounter is extremely small) and the additional energy needed to maintain the powerful emission of radio waves was supplied by the collision.

The existence of such a source suggested at once the possibility of exploring to greater distances, and thus to earlier stages in the history of the universe than would ever be possible in optical astronomy. But before we can use radio observations to test any particular cosmological theory, we must find some quantity which we can predict according to the theory, and which we can also measure. One such quantity, as we have seen, is the density of galaxies at different distances—or equally well, the density of radio galaxies. But in this case we have no way of measuring distance directly. If we knew the average power of the sources, we could use their intensities as a measure of distance.

The first problem is therefore to find the power of the sources, so that we can predict, according to a given cosmological theory, the relative number which we should expect to find in a given range of intensity. We can then compare these results with the actual numbers we find from our observations. We must endeavour to make this comparison for the weakest possible sources—for the further we can penetrate in distance, or the further back in the history of the universe we can reach, the greater will be the differences between the predictions of the different cosmological models.

It seemed impracticable to build an instrument of sufficient size by conventional means, but at Cambridge we have developed a new method of obtaining a very large resolving power, by moving a smaller aerial to different positions within a much larger effective aerial. Our new instrument consists of two elements, one of which is 1,450 ft. × 65 ft. and aligned east–west; the other is a smaller aerial 190 ft. × 65 ft. mounted on railway lines 1,000 ft. long running north–south (Fig. 1). The Earth's rotation scans the beam around a 4-deg. strip of sky each 24 hr., the strip being selected by the elevation of the two aerials.

In each set of observations, the moving aerial is driven to the north end of the rails and the observations are recorded (as holes in punched tape) for 24 hr.; we then move the aerial by about its own width and another set of observations is made. After 25 days we have all the information we need to produce a map of the whole 4-deg. strip.

In order to do this, we must make about a quarter of a million calculations, and these are made on *Edsac*, the computer at the Cambridge University Mathematical Laboratory. The output of the com-

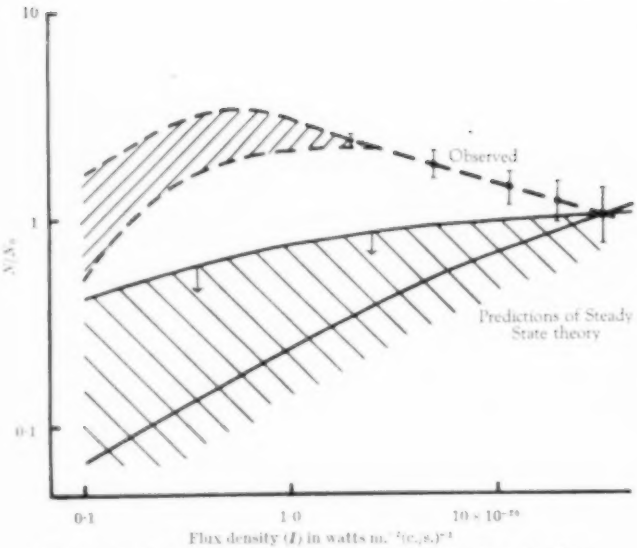

Fig. 2. Plot of relative number of sources observed (N/N_0) above given intensities I. The dotted lines represent the extension of the observations to weaker sources than can be observed individually; they are based on a statistical method which gives no information about the positions or intensities of individual sources, but allows limits to be set to the number of sources of different intensities. The full lines are the curves predicted by the Steady-State model for two values for the effective power of the sources

puter is printed on sheets which enable us to find the positions and intensities of the sources, and the detail obtained is the same as if we had built two aerials each 800 ft. × 500 ft.

We have been using this telescope continuously since it was completed in the summer of 1958, most of the time on problems relating to the cosmological question.

Our first problem was to establish the power of the sources—so that we could predict the relative number of sources we should expect to find at different intensities. At the same time we must make sure that the observations are not being diluted by large numbers of relatively weak sources at small distances—for we know that some of the sources are the remains of supernova explosions inside our own Galaxy—and others are nearby galaxies with relatively weak radio emission.

We have used three methods of finding the power of the sources, the first of which is based on radio methods alone, and involves no assumptions about the nature of the sources. This method showed that only a few per cent of the observed sources were within the Galaxy, and that most of them were external galaxies having a radio emission at least 1,000 times greater than that of our own Galaxy. If we suppose that most of the sources emit as much optical radiation as our own Galaxy, then the limiting optical brightness of the sources allows us to set an even greater limit to the radio emission. The third method was based on measurements of the angular diameters of the sources, and again indicated an average radio emission 10^4–10^5 times that of the Galaxy. From these results we can now compute the number of sources we should expect to find at different intensities; but before we can compare the results with what we observe, we must explore a number of possible difficulties which might affect the interpretation of the observations. One difficulty of this sort is the possibility that radio galaxies might occur in clusters—if they did so, then although we would be able to recognize the individual sources in a nearby cluster, a very distant cluster might be mistaken for a single nearby source. We therefore made a number of subsidiary investigations of this sort to see what corrections would be necessary.

The final, and most extensive problem was to determine the actual number of sources above given intensities, down to the smallest value we could reach. The results, plotted as the number N compared with the number N_0 which would have been observed in the absence of effects of the red-shift, are shown in Fig. 2. The corresponding curves predicted by the Steady-State model on the basis of (*a*) the lowest permissible value of radio power, and (*b*) the value suggested by the optical data, are also shown in Fig. 2; the discrepancy seems too great to be explained by errors in the observations or their interpretation, and suggests that the Steady-State theory in its original form does not correspond to the actual universe.

This is only the beginning of the problem, and the simplest of the questions which one can ask. There are many versions of evolving cosmologies, and there may be special cases of the Steady-State model which fit the present results. More detailed observations may make it possible to eliminate some of these too.

CONTINENT AND OCEAN BASIN EVOLUTION BY SPREADING OF THE SEA FLOOR

By ROBERT S. DIETZ,
U.S. Navy Electronics Laboratory, San Diego 52, California

ANY concept of crustal evolution must be based on an Earth model involving assumptions not fully established regarding the nature of the Earth's outer shells and mantle processes. The concept proposed here, which can be termed the 'spreading sea-floor theory', is largely intuitive, having been derived through an attempt to interpret sea-floor bathymetry. Although no entirely new proposals need be postulated regarding crustal structure, the concept requires the acceptance of a specific crustal model, in some ways at variance with the present consensus of opinion. Since the model follows from

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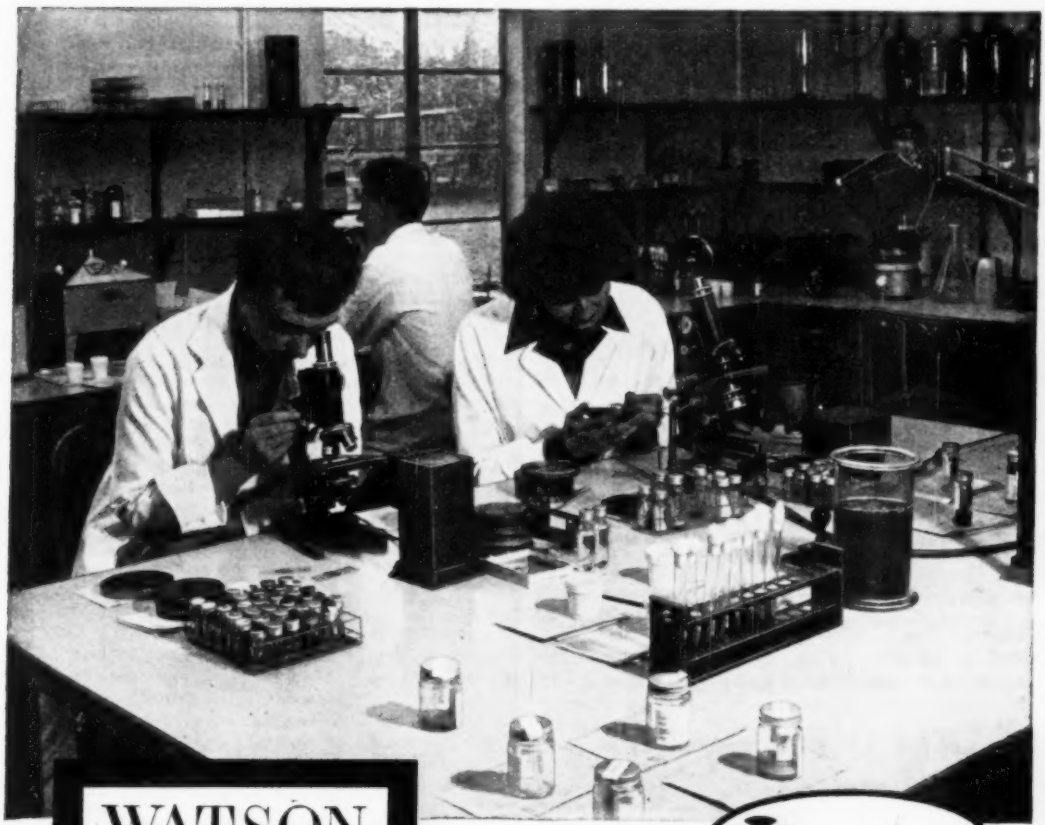

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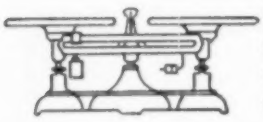

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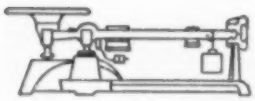

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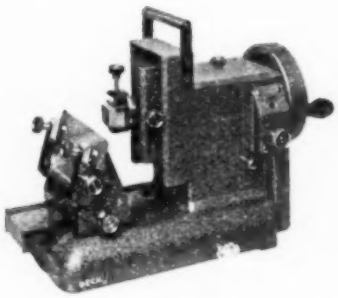

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the concept, no attempt is made to defend it. The assumed model is as follows:

(1) Large-scale thermal convection cells, fuelled by the decay of radioactive minerals, operate in the mantle. They must provide the primary diastrophic forces affecting the lithosphere.

(2) The sequence of crustal layers beneath the oceans is markedly different from that beneath the continents and is quite simple (Fig. 1). On an average 4·5 km. of water overlies 0·3 km. of unconsolidated sediments (layer 1). Underlying this is layer 2, consisting of about 2·0 km. of mixed volcanics and lithified sediments. Beneath this is the layer 3 (5 km. thick), commonly called the basalt layer and supposedly forming a world-encircling cap of effusive basic volcanics over the Earth's mantle from which it is separated by the Mohorovičić seismic discontinuity. Instead we must accept the growing opinion that the 'Moho' marks a change of phase rather than a chemical boundary, that is, layer 3 is chemically the same as the mantle rock but petrographically different with low-pressure phase minerals above the Moho and high-pressure minerals below. This change of phase may be either from eclogite to gabbro[1], or from peridotite to serpentine[2]; its exact nature is not vital to our concept, but we can tentatively accept the eclogite–gabbro transition as it has more adherents. Common usage requires that we reserve the term 'mantle' for the substance beneath the Moho, but in point of fact, the gabbro layer (as a change of phase) is also a part of the mantle—a sort of 'exo-mantle'. Except for a very thin veneer, then, the sea floor is the exposed mantle of the Earth in this larger sense.

(3) It is relevant to speak of the strength and rigidity of the Earth's outer shell. The term 'crust' has been effectively pre-empted from its classical meaning by seismological usage applying it to the layer above the Moho, that is, the sial in continental regions and the 'basaltic' layer under the oceans so that the continents have a thick crust and the ocean basins a thin crust. Used in this now accepted sense, any implications equating the crust with rigidity must be dismissed. For considerations of convective creep and tectonic yielding, we must refer to a lithosphere and an asthenosphere. Deviations from isostasy prove that approximately the outer 70 km. of the Earth (under the continents and ocean basins alike) is moderately strong and rigid even over time-spans of 100,000 years or more; this outer rind is the lithosphere. Beneath lies the asthenosphere separated from the lithosphere by the level of no strain or isopiestic level; it is a domain of rock plasticity and flowage where any stresses are quickly removed. No seismic discontinuity marks the isopiestic level and very likely it is actually a zone of uniform composition showing a gradual transition in strength as pressure and temperature rise; and in spite of the lithosphere's rigidity, to speak of it as a crust or shell greatly exaggerates its strength. Because of its grand dimensions, for model similitude we must think of it as weak[3]. If convection currents are operating 'subcrustally', as is commonly written, they would be expected to shear below the lithosphere and not beneath the 'crust' as this term is now used.

(4) As gravity data have shown, the continents are low-density tabular masses of sial—a 'basement complex' of granitic rocks about 35 km. thick with a thin sedimentary veneer. Since they are buoyant and float high hydrostatically in the sima, they are analogous to icebergs in the ocean. This analogy has additional merit in that convection of the sima cannot enter the sial. But the analogy gives the wrong impression of relative strength of sial and sima; the continental lithosphere is no stronger than the oceanic lithosphere, so it is mechanically impossible for the sial to 'sail through the sima' as Wegnerian continental drift proposes. The temperature and pressure are too high at the base of the sial to permit a gabbroic layer above the Moho; instead, there may be an abrupt transition from granite to eclogite.

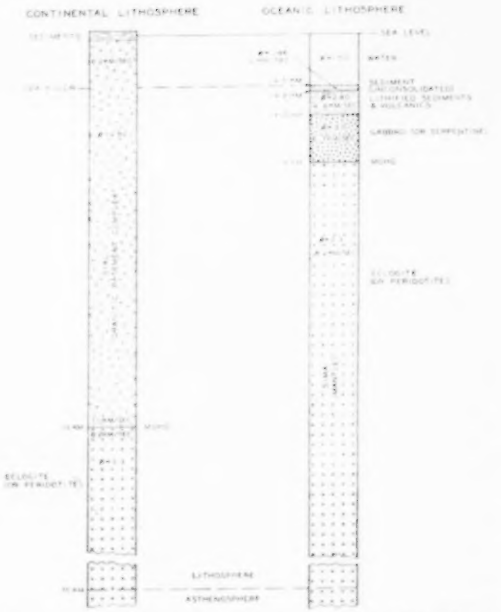

Fig. 1. Generalized crustal sections through the lithosphere beneath the continents and the ocean basins as presumed in this paper. Seismic velocities and densities are shown for the various layers

Spreading Sea Floor Theory

Owing to the small strength of the lithosphere and the gradual transition in rigidity between it and the asthenosphere, the lithosphere is not a boundary to convection circulation, and neither is the Moho beneath the oceans because this is not a density boundary but simply a change of phase. Thus the oceanic 'crust' (the gabbroic layer) is almost wholly coupled with the convective overturn of the mantle creeping at a rate of a few cm./yr. Since the sea floor is covered by only a thin veneer of sediments with some mixed-in effusives, it is essentially the outcropping mantle. So the sea floor marks the tops of the convection cells and slowly spreads from zones of divergence to those of convergence. These cells have dimensions of several thousands of kilometres; some cells are quite active now while others are dead or dormant. They have changed position with geological time causing new tectonic patterns.

The gross structures of the sea floor are direct expressions of this convection. The median rises[4,5] mark the up-welling sites or divergences; the trenches are associated with the convergences or down-welling sites; and the fracture zones[6] mark shears between regions of slow and fast creep. The high heat-flow under the rises[7] is indicative of the ascending

convection currents as also are the groups of volcanic seamounts which dot the backs of these rises.

Much of the minor sea-floor topography may be even directly ascribable to spreading of the sea floor. Great expanses of rough topography skirt both sides of the Mid-Atlantic Rift; similarly there are extensive regions of abyssal hills in the Pacific. The roughness is suggestive of youth, so it has commonly been assumed to be simply volcanic topography because the larger seamounts are volcanic. But this interpretation is not at all convincing, and no one has given this view formality by publishing a definitive study. Actually, the topography resembles neither volcanic flows nor incipient volcanoes. Can it not be that these expanses of abyssal hills are a 'chaos topography' developed as strips of juvenile sea-floor (by a process which can be visualized only as mixed intrusion and extrusion) and then placed under rupturing stresses as the sea floor moves outward?

The median position of the rises cannot be a matter of chance, so it might be supposed that the continents in some manner control the convection pattern. But the reverse is considered true: conditions deep within the mantle control the convective pattern without regard for continent positions. By viscous drag, the continents initially are moved along with the sima until they attain a position of dynamic balance overlying a convergence. There the continents come to rest, but the sima continues to shear under and descend beneath them; so the continents generally cover the down-welling sites. If new upwells do happen to rise under a continental mass, it tends to be rifted. Thus, the entire North and South Atlantic Ocean marks an ancient rift which separated North and South America from Europe and Africa. Another such rift has opened up the Mediterranean. The axis of the East Pacific Rise now seems to be invading the North American continent, underlying the Gulf of California and California[8]. Similarly, the Indian Ocean Rise may extend into the African Rift Valleys, tending to fragment that continent.

The sialic continents, floating on the sima, provide a density barrier to convection circulation—unlike the Moho, which involves merely a change of phase. The convection circulation thus shears beneath the continents so that the sial is only partially coupled through drag forces. Since the continents are normally resting over convergences, so that convective spreading is moving toward them from opposite sides, the continents are placed consequently under compression. They tend to buckle, which accounts for alpine folding, thrust faulting, and similar compressional effects so characteristic of the continents. In contrast, the ocean basins are simultaneously domains of tension. If the continental block is drifted along with the sima, the margin is tectonically stable (Atlantic type). But if the sima is slipping under the sialic block, marginal mountains tend to form (Pacific type) owing to drag forces.

Implications of the Concept

Ad hoc hypotheses are likely to be wrong. On the other hand, one which is consonant with our broader understanding of the history of the Earth may have merit. While the thought of a highly mobile sea floor may seem alarming at first, it does little violence to geological history.

Volumetric changes of the Earth. Geologists have traditionally recognized that compression of the continents (and they assumed of the ocean floors as well) was the principal tectonic problem. It was supposed that the Earth was cooling and shrinking. But recently, geologists have been impressed by tensional structures, especially on the ocean floor. To account for sea floor rifting, Heezen[10], for example, has advocated an expanding Earth, a doubling of the diameter. Carey's[11] tectonic analysis has resulted in the need for a twenty-fold increase in volume of the Earth. Spreading of the sea floor offers the less-radical answer that the Earth's volume has remained constant. By creep from median upwellings, the ocean basins are mostly under tension, while the continents, normally balanced against sima creepage from opposite sides, are under compression.

The geological record is replete with transgressions and regressions of the sea, but these have been shallow and not catastrophic; fluctuations in sea-level as severe as those of the Pleistocene are abnormal. The spreading concept does no violence to this order of things, unlike dilation or contraction of the Earth. The volumetric capacity of the oceans is fully conserved.

Continental Drift. The spreading concept envisages limited continental drifting, with the sial blocks initially being rafted to down-welling sites and then being stablized in a balanced field of opposing drag forces. The sea floor is held to be more mobile and to migrate freely even after the continents come to rest. The sial moves largely *en bloc*, but the sea floor spreads more differentially.

Former scepticism about continental drift is rapidly vanishing, especially due to the palæomagnetic findings and new tectonic analyses. A principal objection to Wegener's continental drift hypothesis was that it was physically impossible for a continent to 'sail like a ship' through the sima; and nowhere is there any sea floor deformation ascribable to an on-coming continent. Sea floor spreading obviates this difficulty: continents never move through the sima—they either move along with it or stand still while the sima shears beneath them. The buoyancy of the continents, rather than their being stronger than the sima, accounts for this. Drag associated with the shearing could account for alpine folding and related compressional tectonic structures on the continents.

Persistent freeboard of the continents. A satisfactory theory of crustal evolution must explain why the continents have stood high throughout geological time in spite of constant erosional de-levelling. Many geologists believe that new buoyancy is added to continents through the gravitative differentiation from the mantle. Spreading of the sea floor provides a mechanism whereby the continents are placed over the down-wells where new sial would tend to collect, even though the convection is entirely a mantle process and the role of the continents is passive. It also follows that the clastic detritus swept into the deep sea from the continents is not permanently lost. Rather, it is carried slowly towards, and then beneath, the continents, where it is granitized and added anew to the sialic blocks.

Youth of the ocean floor. It follows paradoxically from the spreading concept that, although the ocean basins are old, the sea floor is young—much younger than the rocks of the continents. Marine sediments, seamounts, and other structures slowly impinge against the sialic blocks and are destroyed by underriding them. Pre-Cambrian and perhaps even most Palæozoic rocks should prove absent from the ocean floors; and Mohole drilling should not reveal the great missing sequence of the Lipalian interval

(Pre-Cambrian to Cambrian) as hoped for by some. All this may seem surprising, but marine geological evidence supports the concept.

On his discovery of the guyots of the Pacific, Hess[12] supposed these were Pre-Cambrian features protected from erosion by the cover of the sea. But Hamilton[13] proved the guyots of the Mid-Pacific Mountains were Cretaceous, and these seem to be among the oldest of the seamount groups. In an analysis of the various seamount groups of the western Pacific, I was forced to conclude that none of them was older than mid-Mesozoic. The young age of the seamounts has been puzzling; certainly they can neither erode away nor subside completely. Also, there seem to be too few volcanic seamounts, if the present population represents the entire number built over the past hundred million years or more. The puzzle dissolves if sea floor spreading has operated. Modern examples of impinging groups of seamounts may be the western end of the Caroline Islands, the Wake–Marcus Seamounts, and the Magellan Seamounts[14]. All may be moving into the western Pacific trenches. Seamount *GA*-1 south of Alaska may be moving into the Aleutian Trench[15].

The sedimentary layers under the sea also appear to be young. No fossiliferous rocks older than Cretaceous have yet been dredged from any ocean basin. Radioactive dating of a basalt from the Mid-Atlantic ridge gave a Tertiary age[16]. Kuenen[17] estimated that the ocean basins should contain on an average about 3·0 km. of sedimentary rocks assuming the basins are 200 million years old. But seismic reflexions indicate an average of only 0·3 km. of the unconsolidated sediments. Hamilton[18], however, believes that much of layer 2 may be lithified sediments. If *all* layer 2 is lithified sediments, Hamilton finds that the ocean basins may be Palæozoic or late Pre-Cambrian in age—but not Archæan. But very likely layer 2 includes much effusive material and sedimentary products of sea floor weathering. In summing up, the evidence from the sediments, although still fragmentary, suggests that the sea floors may be not older than Palæozoic or even Mesozoic.

Spreading and magnetic anomalies. Vacquier, V., *et al.* (in the press) recently have completed excellent sea-floor magnetic surveys off the west coast of North America. A striking north–south lineation shows up which seems to reveal a stress pattern (Mason, R. G., and Raff, A. D., in the press). Such interpretation would fit into spreading concept with the lineations being developed normal to the direction of convection creep. The lineation is interrupted by Menard's[6] three fracture-zones, and anomalies indicate shearing offsets of as much as 640 nautical miles in the case of the remarkable Mendocinco Escarpment[19]. Great mobility of the sea floor is thus suggested. The offsets have no significant expression after they strike the continental block; so apparently they may slip under the continent without any strong coupling. Another aspect is that the anomalies smooth out and virtually disappear under the continental shelf; so the sea floor may dive under the sial and lose magnetism by being heated above the Curie point.

By considering an Earth crustal model only slightly at variance with that commonly accepted, a novel concept of the evolution of continents and ocean basins has been suggested which seems to fit the 'facts' of marine geology. If this concept were correct, it would be most useful to apply the term 'crust', which now has a confusion of meanings, only to any layer which overlies and caps the convective circulation of the mantle. The sialic continental blocks do this, so they form the true crust. The ocean floor seemingly does not, so the ocean basin is 'crustless'.

I wish to express my appreciation to E. L. Hamilton, F. P. Shepard, H. W. Menard, V. Vacquier, R. Von Herzen and A. D. Raff for critical discussions.

[1] Kennedy, G. C., *Amer. Sci.*, **47**, 4, 491 (1959).
[2] Hess, H. H., *Abst. Bull. Geol. Soc. Amer.*, **71**, Pt. 2, 12, 2097 (1960).
[3] Griggs, D. A., *Amer. J. Sci.*, **237**, 611 (1939).
[4] Ewing, M., and Heezen, B. C., *Amer. Geophys. Union Geophys. Mon. No.* 1, 75 (1956).
[5] Menard, H. W., *Bull. Geol. Soc. Amer.*, **69**, 9, 1179 (1958).
[6] Menard, H. W., *Bull. Geol. Soc. Amer.*, **66**, 1149 (1955).
[7] Von Herzen, R. P., *Nature*, **183**, 882 (1959).
[8] Menard, H. W., *Science*, **132**, 1737 (1960).
[9] Heezen, B. C., *Sci. Amer.*, Oct. 2, 14 (1960).
[10] Heezen, B. C., Preprints, First Intern. Ocean. Cong., 26 (1959).
[11] Carey, W. S., *The Tectonic Approach to Continental Drift: in Continental Drift—A Symposium*, 177 (Univ. Tasmania, 1958.)
[12] Hess, H. H., *Amer. J. Sci.*, **244**, 772 (1946).
[13] Hamilton, E. L., *Geol. Soc. Amer. Mem.*, **64**, 97 (1956).
[14] Dietz, R. S., *Bull. Geol. Soc. Amer.*, **65**, 1199 (1954).
[15] Menard, H. W., and Dietz, R. S., *Bull. Geol. Soc. Amer.*, **62**, 1263 (1951).
[16] Carr, D., and Kulp, J., *Bull. Geol. Soc. Amer.*, **64**, 2, 263 (1953).
[17] Kuenen, Ph., *Marine Geology* (John Wiley and Sons, New York' 1950).
[18] Hamilton, E. L., *Bull. Geol. Soc. Amer.*, **70**, 1399 (1959); *J. Sed Petrol.*, **30**, 3, 370 (1960).
[19] Menard, H. W., and Dietz, R. S., *J. Geol.*, **60**, 3 (1952).

MOUSE CHIMÆRAS DEVELOPED FROM FUSED EGGS

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THE regulative capacities of an egg can be defined by following the development of either its separated parts (or blastomeres) or of united whole ones. The mammalian egg as an object of experimental embryology has been studied more extensively along the first line of approach[1–6]. It has been shown that the isolated blastomeres of 2-cell and even 4-cell eggs can effect regulation. Normal offspring from 'half' blastomeres were reported in the mouse[2,3] and the rabbit[4–6]. 'Quarter' blastomeres of the mouse egg can develop at least into blastocysts[2,3] and in the rabbit can give rise at least to 9½-day-old embryos[5,6].

The only attempt, so far, to fuse mammalian eggs was reported by Nicholas and Hall[1]. These authors transferred pairs of naked, slightly adhering 1-cell rat eggs. A single embryo developed until term, but as the effectiveness of the union achieved had not been checked, the result was not quite conclusive.

In undertaking the work to be described here, it was decided that the *conditio sine qua non* of experiments

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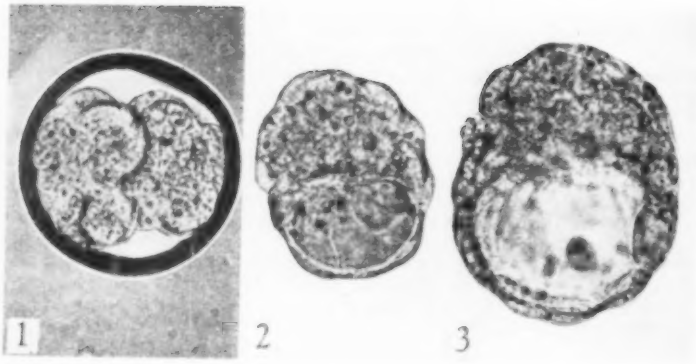

Fig. 1. Two 8-cell eggs compressed in a small drop of medium suspended in liquid paraffin. (×300)
Fig. 2. Single naked blastocyst developed from 8-cell egg cultured for 24 hr. (×400)
Fig. 3. Double blastocyst developed from two fused 8-cell eggs after 24 hr. in culture. (×400)

of this kind was to keep the fused eggs *in vitro* up to the formation of the blastocyst. Moreover, the conditions of culture must be such as to allow the eggs to be observed during development, thus ensuring that all the blastomeres had been incorporated into the one blastocyst.

Work of this type may contribute, as does the other line of approach, to the understanding of the mechanism of normal early development. It should offer, in addition, some new opportunities for research into genetics, developmental genetics and the factors controlling sexual differentiation. Unless eggs from an inbred strain are used, the united components are not genetically identical. In addition, in 50 per cent of cases, sex chimæras would be expected.

The eggs used throughout these experiments were in late phase of the 8-cell stage. The donors were from A_2G albino and *C*57 black inbred strains and from a *LAB* Grey random-breed colony. The eggs of the first two strains were from spontaneous ovulations and the animals were killed in the afternoon of the third day (day when vaginal plug is found is denoted as first day of pregnancy or pseudopregnancy). All the eggs of *LAB* Grey origin were from hormonally induced ovulation in mature animals[7]. Intraperitoneal injection of 3–4 I.U. of pregnant mare serum ('Gestyl') were given, followed after 37–42 hr. by 3–4 I.U. human chorionic gonadotropin ('Pregnyl', Organon Laboratories), and the animals were paired with either *LAB* Grey or A_2G males. Autopsy was performed 78–83 hr. after the second injection. Combinations of eggs united were as follows: (1) $(C57)^2$ + $(A_2G)^2$, (2) $(LAB\ Grey)^2$ + $(LAB\ Grey)^2$, (3) $(LAB\ Grey \times A_2G)$ + $(LAB\ Grey \times A_2G)$, (4) $(LAB\ Grey)^2$ + $(LAB\ Grey \times A_2G)$. It must be added that the offspring from *LAB* Grey × A_2G cross is dark agouti with black eyes, and so in combination (3) both components had the factor for dark pigmentation and in the combination (4) only one of them. As recipients, *LAB* Grey females mated with vasectomized males were used.

The technical procedure comprised: (*a*) removing the zona pellucida, (*b*) joining the eggs, (*c*) culturing, (*d*) transplanting.

(*a*) It was previously reported[3] that the zona pellucida can be removed by mechanical means. The technique was improved for this purpose. A micropipette, with an internal diameter of 65μ, attached by rubber tubing to a compressible rubber bulb was used. The egg was rapidly sucked into the pipette, causing rupture of the zona and allowing the naked egg to escape. The size of the pipette and the suction pressure applied are critical for the success of this operation. All manipulations were carried out under a dissecting microscope. The eggs were under constant observation, and only those with all blastomeres undamaged were used for further work.

(*b*) Two naked eggs were sucked into a pipette and placed with a small drop of medium in liquid paraffin. With another pipette (internal diameter not more than 40μ) attached to a compressed rubber bulb, most of the medium was withdrawn from this drop, thus squeezing the eggs together (Fig. 1). Such pressure was applied for a period of 5–30 min. Several such drops were placed on the bottom of a shallow glass dish treated previously with silicone fluid ('Repelcote', Hopkin and Williams). Up to this moment all manipulations had been carried out in Tyrode's solution with 0·1 per cent bovine plasma albumin, fraction V (Armour).

(*c*) The culture medium was based on that of Whitten (refs. 8, 9 and personal communication). The medium finally adopted consisted of Krebs–Ringer bicarbonate containing per 130 ml. of solution, 2·6 mgm. of phenol red, 4·0 mgm. of both penicillin salt and streptomycin, 400 mgm. of bovine plasma albumin fraction V, and 130 mgm. of glucose. The medium was sterilized by filtration through 'Sterimat' filters (T. B. Fords, Ltd.), in Hemmings bottles, then covered with liquid paraffin and stored at − 20° C. With a sterile pipette, medium was taken through a layer of liquid paraffin and a drop of about 2–4 mm.[3] (though the amount of medium is not critical) placed over each of the small drops containing eggs. The small drop was immediately incorporated into the big one and thus each pair of eggs was cultured separately. More liquid paraffin was added to fill up the dish, which was then covered with a piece of glass. The eggs were cultured at 38° C. Liquid paraffin was gassed before use with 5 per cent carbon dioxide in air, and the *p*H of the medium in the drops immediately adjusted itself to 7·4.

(*d*) The eggs were cultured for 24 or 36–40 hr. and transplanted only after reaching the blastocyst stage. The eggs from the first group (24 hr.) were transferred either to the oviduct on the first day (using the method previously described[10]) or to the uterus on the third day according to the method of McLaren and Michie[11], slightly modified. The eggs kept in culture for 36–40 hr. were transplanted to the uterus only on the third or fourth day of pseudopregnancy. It has been shown previously by McLaren and Biggers[12] that normal 8-cell mouse eggs kept *in vitro* for two days and transferred as blastocysts, develop normally to term, the rate of survival being the same as with untreated controls.

After a few hours in culture, the boundary between the eggs was less clearly defined and in 12–16 hr. each pair had completely rounded up into a single morula, leaving no trace of dual origin. In some of these eggs a small blastocœl had appeared by this

time and after 24 hr. nearly all had developed into early blastocysts. In general, the rate of development was not very uniform and depended on the phase of 8-cell stage used and on the time spent by the eggs at room temperature during the manipulations. After 36–40 hr. the blastocysts were swollen and very large. No strict measurements of the size of 'double' blastocysts nor of single control ones have been made, because of their quick shrinkage at room temperature. The difference in volume of double and single blastocyst was, however, unmistakable, the difference in the size of the inner masses being very conspicuous (Figs. 2 and 3). The lack of the zona pellucida does not affect the size of the naked, single blastocysts, which compare well with their littermates cultured with the zona pellucida intact.

Usually, only a single blastocœlic cavity was formed from the very beginning. Sometimes, however, two distinct cavities appeared, separated either by trophoblastic cells or by the whole bulk of the fused inner masses. With advancing development the two cavities invariably joined together and a perfectly normal blastocyst was formed. In some cases the fusion was not complete, some 1/8 blastomeres or their derivatives being left outside. It was decided, therefore, not to use for transplantation those blastocysts in which more than one 1/8 blastomere (or its equivalent in 1/16 or 1/32 blastomeres) were not completely incorporated.

The general results of the development after transplantation are presented in Table 1. The results concern only those experiments in which eggs of *LAB* Grey origin were used, as no embryo has developed after transferring 19 fused $(C57)^2$ + $(A_2G)^2$ eggs. Among four different combinations of time and type of transfer, only one (line 3) proved to be completely unsuitable. The lack of success was certainly due to the unprepared state of the uterus, which does not allow retention of the eggs.

The first autopsies were performed on the tenth day of pregnancy. At this time, all 6 embryos available were already within the range of normal size variation. A pair of identical twins was also found, the embryos being of different size and retarded approximately 24 and 12 hr. Recipients killed on the twelfth and the fourteenth day yielded 4 (+ pair of identical twins) and 5 embryos respectively. Apart from the twins, all the others fall within the range of normal variation in size.

Of the females left until term, 4 were allowed to litter naturally, the other 4 were killed in the evening on the nineteenth day, the young were removed by Cæsarean section and placed with foster mothers which had littered on the same day, or one or two days before. Although the young seen just after birth and all those seen at the time of Cæsarean section appeared morphologically completely normal and alive, the subsequent mortality-rate was very high. Out of

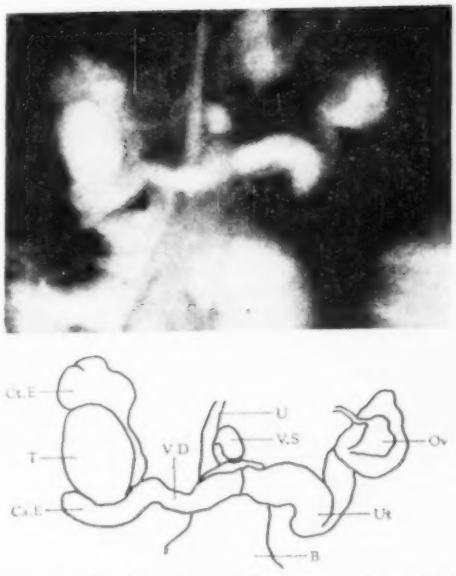

Fig. 4. Photograph (× about 16) of genital apparatus with what appears to be male organs on the left side and female on the right side. The interpretation is given in the key diagram. *B*, bladder; *Ca.E*, cauda epididymis; *Ct.E*, caput epididymis; *Ov*, ovary; *T*, testis; *U*, ureter; *Ut*, uterus; V.D., vas deferens; V.S., vesicula seminalis

10 young littered naturally, none survived. Some of them were partially eaten by their mothers immediately after birth, the others were found dead, though intact, during the first 24 hr. Among 8 young delivered by Cæsarean section, 3 died immediately, 1 survived for 20 hr., 2 for 3 days, and 2 are still alive at the time of writing, being 2 and 5 weeks old respectively. The factors causing this high post-natal mortality are obscure at the moment.

Theoretically, 50 per cent of experimental embryos should be female/male genetical chimæras, 25 per cent males and 25 per cent females. 14 young were available for examination, but only macroscopical details have, so far, been studied. The results of dissection are as follows: 2 females, 9 males and 3 animals with genital apparatus of a clearly mixed type, with a varying degree of intersexuality (Fig. 4). Although the genital apparatus of some other animals classified as males seems to exhibit some deviation from the normal type, nothing more can be said until histological analysis is made. The ratio—2 females, 3 female/male and 9 males—suggests that some of the 'males' are in fact also sex chimæras in which the male component dominates. In the mouse (as in other mammals) the male gonads begin to differentiate earlier than the female gonads[13]. It is possible to

Table 1. Development of Double Blastocysts after Transplantation

Duration of culturing	Time and type of transplantation	No. of recipients	Total No. of transplanted blastocysts	Implantations	Embryos or young	Successful transplantations
24 hr.	Evening 1st day oviduct	13	63	22	16	8
	Evening 3rd day uterus	7	32	18	13	6
36–40 hr.	Morning 3rd day uterus	7	21	1	1	1
	Morning 4th day uterus	12	37	10	6*	6
	Total	39	153	51 (33 per cent)	36 (38*) (21 per cent)	21 (54 per cent)

* 2 pairs of identical twins.

assume that in the sex chimæras the hormones from the male part of the gonads suppress, to some extent, the development of female characters. On the other hand, the 3 clear cases of intersexes, mentioned above, exclude the possibility of complete dominance being an absolute rule. However, nothing is known at present about the distribution in the embryo of the cells derived from the two-component eggs. It seems more likely that the contribution from these two sources to different regions of the body, or even of the organs, is not uniform and varies from individual to individual. The genital apparatus can provide a clear indication of irregularities of this kind. The inconstant genetical constitution of the tissues contributing to this apparatus, when influenced by secondary stimuli, could produce a variety of abnormalities.

The striking ability of mouse eggs to unite and develop into one blastocyst, at so late a stage as the 8-cell, can be accounted for on the basis that the position of the cells is not yet determined. It is during the succeeding mitotic cycle that the trophoblastic cells (or strictly speaking enveloping cells) move and overgrow the cells of the inner mass[14,15]. The movements of enveloping cells must be caused by differing surface activities of the two kinds of cells. In the case of fused eggs, these movements are influenced by the presence of two groups of cells of the inner mass. Consequently, the enveloping cells tend to overgrow the two inner masses together, leaving free from the beginning, or retreating afterwards from, the surface between them. The observations made just after joining and during the first few hours of culturing support this hypothesis. The mechanical squeezing is applied for a short time and results only in approximation of the eggs. Though sticking together, the eggs represent at this time two distinct entities. It is during culturing, when no mechanical squeezing is applied, that the boundary gradually vanishes and real union takes place. The 8-cell stage is the latest convenient stage for this purpose. Eggs joined at the 12-cell stage do adhere together, but later almost invariably separate completely to form two blastocysts.

The perfect morphology of 'double' blastocysts would seem to preclude the possibility that the descendant cells of only one egg contribute to the developing embryo. It will be possible, perhaps, to obtain in future additional proof on purely genetical grounds. In the present work one combination of fused eggs—$(LAB\ Grey)^2 + (LAB\ Grey \times A_2G)$—offers a possibility of tracing the existence of one component due to its factor for pigmentation. It can be assumed that if the pigment were revealed in some form in all or at least in the majority of cases, this could be considered as indirect evidence that the non-pigmented component is also present. As all but one of the young died before the time when skin pigmentation appears, the only criterion available was the eye colour. Among 15 embryos and young, 14 had black eyes, including both embryos in one pair of identical twins. The one additional animal which has survived has black eyes and a uniform coat of the type of the hybrid component.

Briefly, the evidence for real chimærism in the experiments described is three-fold: (1) complete union of two eggs into one blastocyst as seen in culture *in vitro*; (2) the presence of intersexes; (3) the presence of black pigment in the majority of embryos developed from pigmented + non-pigmented fused eggs.

Experiments are still in progress and a detailed account will be published elsewhere.

This work was done during the tenure of a Rockefeller Foundation fellowship. I wish to thank Prof. F. W. Rogers Brambell for allowing me to use the facilities of this laboratory and for his interest and encouragement.

[1] Nicholas, J. S., and Hall, B. V., *J. Exp. Zool.*, **90**, 441 (1942).
[2] Tarkowski, A. K., *Nature*, **184**, 1286 (1959).
[3] Tarkowski, A. K., *Acta Theriologica*, **3**, 191 (1959).
[4] Seidel, F., *Naturwiss.*, **39**, 355 (1952).
[5] Seidel, F., *Naturwiss.*, **43**, 306 (1956).
[6] Seidel, F., *Wilhelm Roux' Arch für Entw. Mech. Org.*, **152**, 43 (1960).
[7] Fowler, R. E., and Edwards, R. G., *J. Endocrin.*, **15**, 374 (1957).
[8] Whitten, W. K., *Nature*, **177**, 96 (1956).
[9] Whitten, W. K., *J. Endocrin.*, **16**, 80 (1957).
[10] Tarkowski, A. K., *Acta Theriologica*, **2**, 251 (1959).
[11] McLaren, A., and Michie, D., *J. Exp. Biol.*, **33**, 394 (1956).
[12] McLaren, A., and Biggers, J. D., *Nature*, **182**, 877 (1958).
[13] Brambell, F. W. R., *Proc. Roy. Soc.*, B, **101**, 391 (1927).
[14] Dalcq, A. M., *Proc. Kon. Nederl. Akad. Wet.*, Ser. C, **54**, 351 and 469 (1951).
[15] Dalcq, A. M., *Introduction to General Embryology* (Oxf. Univ. Press, 1957).

OBITUARIES

Maurice, Duc de Broglie, For.Mem.R.S.

Maurice de Broglie, who died on July 14, 1960, was one of that small band of scientists who pursue their researches privately with their own means. In some respects he was unique. Not only did he establish a laboratory for his own research in his Paris home, but he also collected around him a group of younger men who worked under his guidance. His brother, Louis de Broglie, joined him shortly before the First World War, and much of the initial inspiration of Louis's work came from Maurice's influence. Louis Leprince-Ringuet, Jean Trillat, Jean Thibaud, Alexandre Dauvillier, Bruno Rossi, were among those in his research school. It was his achievement to establish a private research centre of world-wide reputation in his mansion in the rue Chateaubriand.

Maurice de Broglie was born on April 27, 1875, in Paris. He entered the Ecole Navale in 1893 and served for ten years in the Navy. When he left it, in 1902, he established a small laboratory in his house. He was, at that time, interested in the electrical charges on fine particles suspended in an ionized gas, and studied these movements in an electric field, the method afterwards used by Millikan to measure the electronic charge. In 1913 he was one of the first to study X-ray spectra and X-ray absorption. He developed a spectrometer in which he registered, on a photographic plate, the reflected rays from a lattice plane of a slowly rotating crystal. I remember that time well, because Maurice de Broglie and my father corresponded so regularly and compared their results.

During the First World War, he had a commission in the French Navy and made a considerable con-

tribution to the underwater detection of submarines and the development of radio.

After the War, de Broglie continued his researches on X-ray absorption discontinuities, and published, with his brother Louis, *La Physique des Rayons X*, which was a well-known standard work at that time. The laboratory was greatly enlarged and the number of research workers increased. De Broglie's interests turned towards nuclear physics, and some of the devices for observations of high-energy particles which have now become classical were first developed by de Broglie's team. He was elected to the Académie Française in 1934. For ten years he was president of the Conseil Scientifique de l'Energie Atomique.

De Broglie won the warm affection of his students and his many friends all over the world, who will retain pleasant memories of their visits to his home and laboratory, where he was the kindest and most genial of hosts.

W. L. Bragg

Prof. E. Henriot

With the death on February 1 of Emile Henriot, Belgian science lost one of its foremost representatives. Although of French origin (he was born in Besançon in 1885), he spent practically his entire scientific life in Belgium as professor of physics in the Université Libre de Bruxelles and was made emeritus professor in 1956. He suffered in the last few years from ill-health, which fortunately did not diminish in any manner his lucidity or his mental powers.

Among his many contributions to physics, two stand out by which his name will be remembered. The first was the subject of his doctor's thesis. By a masterly series of investigations, he was the first to show definitely that potassium and rubidium are naturally radioactive. This work, done before the First World War, was an investigation in the best tradition of the great French school of radioactivity measurements.

In more mature years came his justly famous investigations of extremely high angular velocities. He found that suitably placed air-jets can be used to spin tops at very high speeds, and he developed this technique to the point where it could be used for certain physical measurements. Although he originally wanted to use it for a precision determination of the speed of light, in the hands of Beams these air-driven tops became the mechanism of the then most successful ultracentrifuges.

Henriot was attracted time and again to questions of optics, where he was able to use his great theoretical skill. Problems of birefringence and molecular vibrations have been treated very successfully in several of his papers.

His contributions to physics went considerably beyond his own research. He was an outstanding teacher, and several of his former pupils are now professors of physics in different places. To the physics community at large, he was known as the organizer of the physics conferences of the Solvay Institute. For more than thirty years, he was a member of its administrative committee and for about twenty years he was its secretary. To the physicists going to these conferences he was a familiar figure, and he succeeded in maintaining these conferences at a very high level.

Physics was not his only love. Everything human attracted him, and his friends could, and did, learn much from him about art or archæology. He had a fine collection of Greek marbles and a beautiful library adorned by many valuable books. Moreover, he was an extremely warm human being, and those who had the good fortune of being his friends deplore his death.

The many distinctions which came to him were never mentioned by him. He was a very modest person, modest almost to shyness. He married one of his former students, who became his collaborator for very many years. During the Second World War, Henriot was professor at the University of Algiers, when evacuated from Belgium and France. By coincidence, his daughter still lives there. In the opinion of some of his colleagues, the good physics tradition in Algiers really started with his teaching there.

All his friends and the world of physics will miss him.

L. Marton

Mr. G. W. G. Briggs

Guy Briggs, assistant director of the National Institute of Agricultural Botany, died in hospital at Cambridge on March 7. His death at fifty-seven brings a deep sense of loss to his colleagues in many countries who shared his interest in problems relating to grassland and to seeds.

His early interest in agriculture developed as he lived during school vacations on his grandfather's farm at Melbourne in Derbyshire. From King's College, Wimbledon, he went to Wye College, where he gained distinction in botany and in agriculture in the diploma examinations.

Entering the Colonial Agriculture Service in 1926, he was in close touch with the experimental farms and with advisory work among the growers. Those who knew him at that time remember the keen personal interest he took in all who sought his assistance, both Africans and Europeans. He played a leading part in the development of the rice crop and he had the satisfaction of seeing Nigeria become self-supporting in this cereal.

Retiring on medical advice from the Colonial Service in 1945, he was appointed as a technical officer at the National Institute of Agricultural Botany, becoming head of the Seed Production Branch in 1948 and assistant director of the Institute during January 1960.

Briggs's great organizing ability was admirably combined with a deep appreciation of technical problems on seed production. The researches of Stapledon and his colleagues at Aberystwyth had shown the value of leafiness and persistence in grasses and clovers, and had led to the development of a series of varieties which possessed these qualities. Briggs played an important part in bringing these to the notice of growers and in helping to develop methods of seed production which enabled the new varieties to be grown commercially on a large scale without losing their distinctive features.

The agricultural industry was beginning to appreciate the value of seed produced under technical supervision, and it was Briggs who was mainly responsible for organizing, on behalf of the National Institute of Agricultural Botany, the national certifying authority for herbage seeds. In this he had the strong support of the Welsh Plant Breeding Station, the seed trade and the National Farmers' Union.

Briggs took an active interest in developments in seed production abroad, and when, in 1958, the Organization for European Economic Co-operation adopted throughout the eighteen member countries an

international scheme for herbage seed certification, experience gained in working the British scheme proved most valuable.

The comprehensive survey Briggs gave in his paper to the International Grassland Congress at Reading in 1960 has led to a better appreciation of the part seeds of high quality can play in the improvement of crop production.

At Cambridge, Guy Briggs was particularly valued for the soundness of his advice, which was always given in the most kindly way. He was able to make friends of those with whom he worked and he has made a big contribution to the good relations which exist between research workers, seedsmen and farmers.

His influence will continue to be felt, both through the work he did and through the help and training he gave to so many others.

Guy Briggs leaves a widow and a son of his first wife, who died in 1945. F. R. Horne

NEWS and VIEWS

New Scientific Attachés : Dr. C. R. S. Manders and Mr. W. F. G. Drury

Dr. Charles Manders has been appointed to the new post of scientific attaché to the British Embassy, Tokyo. He will hold the rank of senior principal scientific officer and joins the Department of Scientific and Industrial Research from the Ministry of Defence. Dr. Manders was educated at King's College, University of London, where he obtained a double first (general and physics). He served in the army during 1941–47, including a two-year spell as a lecturer at the Military College of Science. In 1947 he joined the Scientific Civil Service and for the past ten years has been with the Ministry of Defence on scientific duties. He is interested in education and has a translation of a collection of Soviet technological curricula, and also a translation of a French book on thermodynamics, in the course of publication.

Mr. W. F. G. Drury, scientific assistant to Sir John Carroll, deputy controller (research and development), Royal Naval Scientific Service, has been appointed scientific attaché to the British Embassy in Stockholm, in succession to Mr. G. H. Greenhalgh. He was educated at University College School, Hampstead, and on leaving school at 18, joined the Electrical Research Association as a technical assistant. He entered the Civil Service two years later, and during 1938–53 he was at the Admiralty Signal School, working mainly on radar and radio research and development projects. In 1953 he was appointed to the British Joint Service Mission in Washington. He returned to the Admiralty Signal Research Establishment in 1955 and was appointed to his present post in 1956.

Pharmaceutical Chemistry in London: Prof. W. H. Linnell

Prof. W. H. Linnell, who is retiring from the chair of pharmaceutical chemistry in the School of Pharmacy, University of London, was appointed to the staff as reader in 1926 and to the chair of pharmaceutical chemistry in 1949. He had previously studied at the University of Durham, 1919–23, and, following the award of the Earl Grey Memorial Fellowship, at Lincoln College, Oxford. He afterwards had experience as a member of the research staff of H.M. Fuel Research Station. In 1956, while retaining the chair of pharmaceutical chemistry, he was appointed dean of the School of Pharmacy in succession to Prof. H. Berry. He is a member of the British Pharmacopœia Commission and the Revision Committee of the British Pharmaceutical Codex. In 1960 he was chairman of the British Pharmaceutical Conference at Newcastle upon Tyne. Prof. Linnell has been responsible for the development of the new subject of pharmaceutical chemistry in the School, and his own research work has been mainly in the field of chemotherapy.

Prof. W. B. Whalley

Dr. W. B. Whalley has been appointed to the chair of chemistry created on Prof. Linnell's retirement from the chair of pharmaceutical chemistry at the School of Pharmacy, University of London. Throughout his academic career, Dr. Whalley has been associated with the University of Liverpool. After taking the Ph.D. degree in 1940 he worked in the Research Department of the General Chemicals Division of Imperial Chemical Industries, Ltd., at Widnes. A few years later he returned to Liverpool and began a long and productive collaboration with Prof. Alexander Robertson. Together they investigated successfully the structures of many natural products, especially complex heterocyclic compounds of oxygen. However, the most notable development was the study of fungal metabolites with varied structures, many of which were elucidated. Citrinin, rosenonolactone, and the novel class of pigments typified by sclerotiorin are good examples. Since Prof. Robertson's retirement in 1957, Dr. Whalley has continued energetic work with fungal metabolites, partly in collaboration with Dr. J. S. E. Holker, and he has turned his attention to their biosynthesis. Dr. Whalley's research interests have extended to other fields, and his numerous publications include several valuable review articles. In 1952 he spent six months at Smith, Kline and French Laboratories, Philadelphia. At Liverpool, where he has been reader since 1957, Dr. Whalley's work has not been confined to the Organic Chemistry Department. He is at present senior tutor of the Faculty of Science, and for some years he has been prominent in educational circles in Merseyside as a school governor, extra-mural lecturer, etc. Dr. Whalley's new post will give scope to his talents as an administrator, research worker and teacher, and his numerous friends look forward to his success in it.

The Royal Aeronautical Society : Elections and Awards.

Air Marshal Sir Owen Jones has been elected president of the Society. He has served on the Council since 1955 and was a vice-president of the Society during 1957–60. *Honorary Fellowship* of the Society has been conferred on Sir Sydney Camm, director and chief engineer, Hawker Aircraft, Ltd., and J. D. North, chairman and managing director, Boulton Paul Aircraft, Ltd. *Honorary Companionship* of the Society has been awarded to J. N. Toothill, director, Ferranti, Ltd., Hollingwood, Lancashire, and general manager, Ferranti, Ltd., Edinburgh.

At the annual general meeting of the Society held on May 4 the following awards were announced: *Simms Gold Medal*, to Prof. D. B. Spalding for his paper, "Heat and Mass Transfer in Aeronautical Engineering"; *George Taylor (Australia) Gold Medal*, to A. J. Troughton for his paper, "Relationship between Theory and Practice in Aircraft Structural Problems"; *Edward Busk Memorial Prize*, to C. Bourque and Prof. B. G. Newman for their paper, "Reattachment of a Two-dimensional, Incompressible Jet to an Adjacent Flat Plate"; *Orville Wright Prize*, to Prof. W. H. Wittrick for his paper, "Analysis of Stress Concentrations at Reinforced Holes in Infinite Sheets"; *Herbert Akroyd Stuart Memorial Prize*, to J. S. Alford, for his paper, "Power Plants for Supersonic Transports"; *Branch Prize*, to Lieut. Commdr. D. J. Whitehead for his paper, "The Low Speed Approach and Catapult Launch Problems in High Performance Naval Aircraft"; *Usborne Memorial Prize*, to T. W. F. Moore for his paper, "Some Experiments on the Reattachment of a Laminar Boundary Layer separating from a Rearward Facing Step on a Flat Plate Aerofoil".

The Society has also announced the following awards: *Silver Medal*, to R. Hafner, technical director (research), Westland Aircraft, Ltd., for outstanding work in the design and development of rotary-wing aircraft; *Bronze Medal*, to L. Haworth, assistant chief engineer, Propeller Turbines, Rolls-Royce, Ltd., for his work leading to advances in aircraft gas-turbine design; *British Gold Medal for Aeronautics*, to Dr. S. G. Hooker, technical director (Aero), Bristol Siddeley Engines, Ltd., for outstanding achievement in aero-engine design and development; *R. P. Alston Medal*, to R. P. Dickinson, superintendent, Aeroplane and Armament Experimental Establishment, Boscombe Down, for his achievement in the execution and direction of flight test observation work; *Wakefield Gold Medal*, to Dr. E. Eastwood, director of research, Marconi's Wireless Telegraph Co., Ltd., for his contributions to the development of air traffic control and navigational aids; *British Silver Medal for Aeronautics*, to Pierre Satre, technical director, Sud-Aviation, Paris, for his work on aircraft design, with special reference to his development of the rear-engined configuration. *N. E. Rowe Medals*, for younger members of the Society, and awarded for the best lecture given to any Branch of the Society by a member of a Branch: 21–26 years age-group, to J. Wilding, of the Chester Branch, for his paper "Bird Flight and the Aeroplane"; under-21 years age-group, to W. Bishop, of the Brough Branch, for his paper "The Development of Tailless Aircraft and Flying Wings".

The Queen Elizabeth II Canadian Medical Fund

Dr. M. W. Partington has been appointed the first "Queen Elizabeth II Scientist" by the Queen Elizabeth II Canadian Fund to Aid in Research on the Diseases of Children; the Fund was established by the Federal Government of Canada to mark the occasion of Her Majesty's visit to Canada in 1959. Dr. Partington, a Research Fellow in neurology at the Research Institute of the Hospital for Sick Children, Toronto, will take up his new post on July 1 in the Department of Pædiatrics at Queen's University, Kingston, where a permanent research unit will be set up to initiate, foster and carry out research on pædiatric problems, such as mental deficiency and epilepsy in children. Three "Queen Elizabeth II Fellowships", totalling 13,500 dollars, were also awarded to: Dr. John Alexander Lowden, to continue studies towards a Ph.D. degree in biochemistry at McGill University, under Drs. K. A. C. Elliott and L. S. Wolfe; Dr. George Greenough Hinton, research fellow in neurology at the National Hospital for Nervous Diseases and Hospital for Sick Children, London (England), to work at the War Memorial Children's Hospital and the Psychiatric Research Centre, London (Ontario), under Drs. J. C. Rathbun and D. Zarfas; Dr. Hugh Taylor, chief resident of the Children's Hospital, Winnipeg, to work in the Department of Pediatrics, New York University, under Drs. J. Dancis and S. Krugman.

Science in Society

The impact of scientific and technological progress on society is being examined in more than 200 research projects in the colleges, universities, and other institutions in the United States. These studies are described in a newly released issue of the National Science Foundation publication, *Current Projects on the Economic and Social Implications of Scientific Research and Development*, 1960 (Pp. v+124. Washington, D.C.: Government Printing Office, 1961. 40 cents). The effects of science and technological progress are examined in relation to such subjects as agriculture, impact on selected industries, administration and management, and labour. Other factors being studied are patents, scientific man-power and creativity, and science policy. Each project is summarized and listed with the names of the investigators, address of institution, and the anticipated form of publication of results. The first issue of this publication covered the year 1959. During 1959–60 the number of projects reported to the Foundation more than doubled.

Bibliography of Influenza

The American Institute of Biological Sciences has issued the first of a new quarterly publication containing a bibliographical record of articles published on influenza and related subjects in the United States and elsewhere (*An Annotated Bibliography of Influenza*, Vol. I, No. 1; September 1960. Pp. 20. Published quarterly. Washington, D.C.: American Institute of Biological Sciences, 2000 P Street, N.W., 1960). Approximately 2,600 journals are being examined for information. Each issue of this bibliography is divided into the following major categories: general and review; epidemiology; clinical; pathology; prophylaxis; immunology; virology; and animal studies.

The Smithsonian Institution

Bulletin No. 220 of the United States National Museum is a list of type specimens of reptiles and amphibians in the Museum (*Type Specimens of Reptiles and Amphibians in the U.S. National Museum*. By Doris M. Cochran. Pp. xv+291. Washington, D.C.: Government Printing Office, 1961. 1.25 dollars). It has been compiled by Miss Doris M. Cochran, curator, and contains 1,742 names. An interesting introduction reviews the history of the collections and is followed by the list giving the original genetic, specific and sub-specific names. The name of the author is added and also the name of the publication where the name and description first appeared. Afterwards, if the original name of the genus or species is no longer accepted, the present

synonym is added in italics. A comprehensive index completes the monograph.

Eye Examinations of Asian School Children

The eyes of 359 children attending the Indian public primary school in Mwanza have been examined by members of the Biochemistry Nutrition Division of the East African Institute for Medical Research (Report, 1959–60. Pp. ii+36. Mwanza: East African Institute for Medical Research, 1960. Sh. 3). Apart from refractive errors there was almost no eye disease. Heights and weights were also obtained and all the data have been prepared so that comparison can be made with a similar study made by Pendse (1954) in Poona. This is the first time that refractive errors and growth data have been compared for two closely related communities in different parts of the world. In both height and weight the Gujerat children of Mwanza are superior to the Maratas of Poona. It is postulated that the greater growth of the Mwanza children is due to the improved conditions under which they now live in East Africa. The Mwanza refraction data showed a marked excess of emmetropic and near-emmetropic refractions compared with the normal distribution and also a myopic excess and a prolongation of the myopic tail. When a comparison is made of the percentage distribution of refraction in the Mwanza and the Poona children, close similarity is seen. Mixed astigmatism and anisometropia were present in 6·6 per cent and 8·6 per cent respectively of these children. These figures occupy a position intermediate between those of the Mwanza African children and those for Mvuni African children. About 1 per cent of the children had squint and less than 1 per cent were wearing glasses at the time of the examination. These Asian children were also examined for the presence and degree of water cleft opacities in the periphery of the lens. Comparison of the details shows that the incidence was slightly lower than in the Mwanza African children.

Journal of the Association for Computing Machinery

The January 1961 issue of the *Journal of the Association for Computing Machinery* contains six major papers, at least three of which will be of general interest. The first of these, by Herbert Keller, is an analysis of finite automata with special reference to pattern recognition. The main theme is a description of various 'perceptrons', a mysterious term which for some time has puzzled British users of computers, being claimed by some to hide a concept of deep significance, and by others to be a triviality. Keller takes as his definition something which is usually regarded in Britain as a variety of synthetic neurone, and his analysis of the potentialities of this class of device will, no doubt, stimulate discussion. Ivan Flores contributes a paper which analyses the use of computers as sorting machines. This particular class of operation is one which does not show the machines at their best so that analyses which estimate efficiencies are always useful. Probably the most generally interesting contribution is that by Leiner and Youden on generating pronounceable names on a computer. Their particular names have four letters and an amusing touch is their lament: "... some of the computer-generated words, although highly efficient phonetically, were semantically unsuited for permanent inclusion in the records". It seems that some humans had to draw up a proscribed list before the records were fit for publication.

The Pontide Paradox

According to a number of prominent geologists, the region occupied by the present Black Sea ('Pontus Euxinus' of the ancients), even as late as the second half of the Tertiary era, was occupied by a land mass called Pontide. Furthermore, according to this hypothesis the present Crimean mountains represent the northern fringe of this land mass untouched by a widespread subsidence affecting the greater part of this continent. On the other hand, some geologists query the idea of the existence of Pontide in the late Tertiary era, and their views are supported by M. V. Muratov (*Priroda*, 6, 57; 1960), who, in a series of palæogeographical maps, illustrates the evolution of the future Black Sea from its initial stages to the northern geosyncline of the Tethys. Such a hypothesis also finds its support in the observed peculiarities of the present-day flora and fauna of the Crimea. These biogeographical data, on the other hand, provide N. I. Rubtzov (*Priroda*, 8, 83; 1960) with an additional argument in the support of the hypothesis of the existence of Pontide.

Cultural Sequences in Hokkaido, Japan

Quite a lot is known about the prehistory of China. Pekin man and the stone-age industry found in the cave with his remains have at least given a start for the study of the earliest cultures of that vast region. Again, not a few of the museums in Britain display painted pots of Neolithic date—the earliest of a long line of painted pottery from China. Much less is known about the earliest history of Japan. The article by Lieut.-Col. H. A. MacCord in a recent paper (*Proc. U.S. Nat. Mus.* (No. 3443, Vol. 112): Pp. 481–503 + 14 plates. Washington, D.C.: Government Printing Office, 1960) does not profess to fill this gap, but does describe some research work undertaken during 1953–54 in the island of Hokkaido, in the region of the Ishikari Plain. Pottery, most of it decorated, and stone tools were found, and many of these are illustrated in 14 full pages of half-tones. The stone tools include polished 'celts', knives and arrow heads, some of obsidian. Some day we shall hope to see a volume on Japanese prehistory; the results published here will certainly merit inclusion in all libraries of archæology and ethnology.

The Advisory Group for Aeronautical Research and Development

The Advisory Group for Aeronautical Research and Development announces the following schedule of meetings: June 5–9, Documentation Committee on "Exchange of Information in the Nato Countries" (Paris); July 12–19, Seminar on Astronautics, jointly sponsored by the University of Southampton and AGARD (Southampton); July 18–21, Fluid Dynamics Panel on "The Use of Rocket Vehicles in Flight Research" (The Hague); July 24–26, Avionics Panel Technical Meeting on "Microminiaturization" (Oslo); Structures and Materials Panel Specialists' Meeting of the Material Group (Oslo); July 27–28, 11th AGARD General Assembly, "Scientific Goals of Space Exploration and Research" (Oslo); July 31–August 2, Avionics Panel Technical Meeting on "Low-noise Electronics" (Oslo).

Field Studies Council: Summer and Autumn Courses

The Field Studies Council has announced the programmes of special courses to be held during

1961 at its various Field Centres. *Malham Tarn Field Centre* (near Settle, Yorkshire): grasses, sedges and rushes (July 5–12); mosses and liverworts (August 23–30); identification and ecology of lichens (August 30–September 6); ecology of freshwater animals (August 30–September 6); meteorology, organized in conjunction with the Royal Meteorological Society (September 6–13); fungi (September 6–13); Pennine fossils (September 13–20); rivers and streams (September 20–27); karstic land-forms (September 20–27); spider ecology (September 20–27). *Flatford Mill Field Centre* (East Berghold, near Colchester, Essex): art of botanical illustration (July 19–26); landscape painting courses (August 9–23); animal life in the soil (August 9–16); insect ecology (August 16–23); field archæology (August 23–September 6); small mammals (September 16–23); autumn art week (October 4–11). *Slapton Ley Field Centre* (Slapton, Kingsbridge, Devonshire): outdoor painting course (August 9–16); natural history fortnight (August 9–23); introduction to the study of lichens (August 16–23); introduction to the study of seaweeds (August 16–23); natural history of south-western woodland (August 30–September 6); geology and scenery for beginners (August 30–September 6); introduction to the study of lower plants (September 20–27). *Dale Fort Field Centre* (Haverfordwest, Pembs.): weather and bird movements, organized under the auspices of the Royal Meteorological Society and the British Trust for Ornithology (September 6–13). Further information on each of the courses can be obtained from the Warden of the Field Centre concerned.

Keele Foundation Year Course

The Nuffield Foundation has made a grant of £5,000 to the University College of North Staffordshire to pay for an investigation into the effects of the Keele Foundation Year course. This course, unique to Keele, is taken by all students in the first year of the four-year degree course and is designed to introduce the student to some of the methods and information necessary to an estimate of the inheritance, the problems and the achievements of modern western European man. The grant will pay the salary of a Research Fellow and an assistant who will attempt to establish any relationship there may be between performance in the Foundation Year course and such factors as previous educational record, subsequent performance in the degree course, career after graduation, etc. It is hoped that the information obtained may give valuable indications of ways in which the Foundation Year course can be further developed or modified and that this may be the first stage of a continuing inquiry.

Announcements

The Meldola Medal for 1960 has been awarded to Dr. J. N. Bradley, for his work in the field of physical chemistry, with special reference to the kinetics of reactions involving free radicals and reaction in shock waves studied by mass spectrometry. The award is made by the Royal Institute of Chemistry with the concurrence of the Society of Maccabaeans.

Dr. R. Conrad, assistant director of the Medical Research Council's Applied Psychology Research Unit at Cambridge, will act as consultant in applied psychology to the General Post Office for an initial period of two years.

At a meeting held on May 11, the Council of the Association of British Chemical Manufacturers appointed Mr. H. W. Vallender as deputy director of the Association.

The following appointments at the U.N. Food and Agriculture Organization have been announced: Dr. Hans Dietrich Cremer, to be chief of the Applied Nutrition Branch; Dr. Arthur H. Dolff, to be assistant chief of the Research Branch of the Radiological Health Division.

The sixteenth annual electronics, instruments and components exhibition and convention of the Institution of Electronics will be held at the College of Science and Technology, Manchester 1, during the periods July 6–8 and 10–12 inclusive. This programme will incorporate a scientific and industrial research section, a manufacturers' section and a number of lectures and films. Further information can be obtained from the general secretary, W. Birtwistle, Institution of Electronics, 78 Shaw Road, Rochdale, Lancs.

The Department of Mathematics of the Hatfield College of Technology is organizing a summer school on "Mathematics of Automatic Control" during June 26–30, the object being to enable mathematicians and engineers working on problems of automatic control to study some of the relevant mathematical techniques developed in recent years in Britain, America and the U.S.S.R. Further details can be obtained from the Academic Registrar, Hatfield College of Technology, Hatfield, Herts.

The annual meeting of the American Society of Pharmacognosy will be held at the University of Houston during June 19–21. Among the subjects to be considered are: opportunities for Ph.D. pharmacognosists; specific techniques of thin-film chromatography; uridine nucleotides in glycoside biosynthesis; chemo-taxonomy of selected groups within the Coniferae; research on south-western drug plants; the pharmacognosy of the anti-cancer plants, the periwinkles. Further information can be obtained from Melvin R. Gibson, School of Pharmacy, Washington State University, Pullman, Washington.

Elliott Brothers (London), Ltd., a member of the Elliott-Automation Group, is organizing a private symposium and exhibition on "Analytical Instrumentation of Industrial Process Control" at the Connaught Rooms, London, during June 13–14. Included will be papers on: the application of analysis instruments in the United States; the continuous measurement of moisture; analysis instruments from the point of view of the user; experience with plant stream analysers at Imperial Chemical Industries, Ltd., Billingham; trends in continuous process analysis. The exhibition will include a selection of 'Quality Control' instruments supplied by the Analytical Instruments Division of Elliott Brothers (London), Ltd., Further information can be obtained from John Geddes, Elliott-Automation, Ltd., 34 Portland Place, London, W.1.

Errata. The following corrections are necessary in the communication entitled "Minimum Range to Artificial Earth Satellites" in *Nature* of April 22, p. 333. In the first line of the paragraph containing equation (5), for "$\rho_s = \rho_s = \infty$" read "$\rho_s = \rho_p = \infty$". Further, the numerator on the left-hand side of equation (5) should read "$\lambda(f')_{f=f}$"; in some copies the differentiation sign has not registered.

ELECTRICAL CONTACTS

A SYMPOSIUM on "Electrical Contacts", organized by the Institute of Physics and the Physical Society, in collaboration with the Institution of Electrical Engineers, was held during April 5–7, at Brunel College of Technology. The membership was limited to some 260 by the accommodation only, and interest in the subject was such that acceptances were closed some weeks before the date of the symposium, which, although not meant to be international in character, was, nevertheless, attended by representatives from a dozen different countries. The subject under consideration, being of fundamental scientific interest as well as of obvious practical significance, proved itself to be of concern to physicists, engineers, metallurgists and chemists from both industrial and Government research establishments as well as universities. The symposium was so arranged that the main aspects of electrical contact phenomena could be discussed in some detail in separate sessions.

The opening session consisted of an address by Prof. F. Llewellyn Jones (University College of Swansea) on "The Physics of Electrical Contact Phenomena", in which the main aspects of contact operation were surveyed, and the important problems of fundamental significance indicated, as well as the methods by which they are now being attacked in the various laboratories. The sessions which followed each consisted of between four and six short papers grouped under the headings: principles, fundamental investigations and techniques, contact surfaces, methods and design, non-metallic contacts, and miscellaneous subjects. Each session included a discussion. In this brief communication it is not possible to give an account of all twenty-five papers in detail; a fuller report is being published in the *British Journal of Applied Physics*. This notice will be confined to comments on the scope of the discussion and the general conclusions reached.

The opening survey address considered the whole contact operation from the initial approach to the final separation of the electrodes, in the order in which the events usually take place. The aspects concerning fundamental physics and some of the problems still unsolved were pointed out. For example, the behaviour of a contact just before the electrodes actually touch ($\sim 10^{-4}$ cm. apart) involves interesting problems of surface physics relating to the electrical activity of surfaces due to the presence of thin films. Attention was also directed to the interesting and varied phenomena associated with molten, and possibly boiling, metal in the microscopic region of contact. In this connexion, contact physics can make a contribution to our knowledge of the properties of metals at high temperatures in the molten state. A ciné-film was exhibited, showing the quasi-static molten metal bridge passing through a series of mathematically predictable shapes before sudden breaking. The establishment of a micro-arc immediately on the breaking of the bridge was then considered, and the possibility of ionic transfer in the high-temperature plasma pointed out. Finally, the importance of surface films was referred to in the operation of very light-duty contacts with negligible currents—the electro-static contacts.

In the second session dealing with principles, the theme of the properties of metals at high temperatures was further developed by Dr. M. R. Hopkins (University College of Swansea). Thermal instability in a contact was discussed by Dr. J. B. P. Williamson (Cavendish Laboratory and Tube Investments, Ltd., Cambridge). Because of the importance of the nature and behaviour of surface films on contact electrodes (continually emphasized during this conference), the mechanism of formation of oxide films on metals was considered by Dr. O. Kubaschewski (National Physical Laboratory). Interest in non-metals was illustrated by a paper on the friction and wear of graphitic and non-graphitic carbon in which the important rule of adsorbed layers was stressed by Dr. J. W. Midgley (English Electric, Ltd., Leicester).

In the third session, the different techniques of investigations of the various aspects of contact operation were described. P. E. Watts (Associated Electrical Industries, Aldermaston) showed how the effect of temperature asymmetry on matter transfer was being investigated, while Dr. C. H. Jones (Royal Marsden Hospital) described the work done at the Department of Physics, University College of Swansea, using radioactive tracer techniques for the measurement of metal transfer. This sensitive method enables the transfer in an opening contact to be measured with very low series inductances, and it was concluded that transfer in platinum, palladium and silver was not independent of the micro-arc discharge. Dr. A. Fairweather (Post Office Research Station) illustrated the properties of the mechanical deformation of contact electrodes at closure by means of models in two-colour laminated 'Plasticene'. He showed that different forces produce geometrically similar indentations, and that the flow-patterns depend on frictional constraints.

Most of the remainder of the session was devoted to the properties of contact surfaces. The practical aspects of very light-duty electrical contacts were assessed in a review paper by Dr. J. C. Chaston (Johnson Matthey, Ltd., London). From the practical point of view of design and manufacture important factors were electrode shape and material, surface finish, contact-loading force, and in particular the separating force and freedom from bounce.

The cleanliness of precious metal surfaces was discussed by H. C. Angus, while Dr. W. Betteridge (both of International Nickel Co. (Mond), London) considered the operation of extremely light-duty contacts at high temperatures. For example, at temperatures of 500° C. contact operation can become difficult because of oxidation, welding and thermo-electric effects. So far as noble metals are concerned, investigations show that gold and platinum are film-free, but that ruthenium has a highly conducting oxide. Electro-deposition of metals was described in some detail by F. H. Reed (International Nickel Co. (Mond), London), and other papers provoked much further discussion on this topic. Quanti-

tative assessment of electrode activity due to surface films was described by E. B. Pattinson (Department of Physics, University College of Swansea) and the influence of dust on contacts was considered by Dr. J. A. Greenwood (Tube Investments, Ltd., Cambridge). Dr. Fairweather discussed the effects of plastic lubricants and the behaviour of granular materials. With these materials, energy losses depend not only on the properties of the material but also on granule dimensions and the structure of the granular boundaries. A description of recent contact research in Japan was given by Prof. G. Matsumoto (Tohoku University). The properties of electrodes of silver–nickel and silver–metallic oxides, produced by powder metallurgy, were described, as well as work on arc suppression by electro-chemical treatment of the electrode surfaces. The selection of electrical contact materials for light-duty applications was surveyed by Dr. V. G. Morradian (Engelhard Industries Inc., New Jersey). The proceedings closed with a summary by Dr. M. R. Hopkins.

The last conference on electrical contacts in Britain was held in 1952 (see *Nature*, **169**, 960; 1952), and it is interesting to consider the developments which have occurred since then. Despite hopes that recent developments in electronics, particularly in the field of semi-conductors, might avoid difficulties associated with conventional metal-to-metal contacts, it is clear that basic problems in electrical contacts are still with us. Some practical problems have been solved, or circumvented, but others have appeared in new forms. However, considerable advances have been made in our knowledge of the physics of the molten metal bridge, its formation, growth and final destruction, and of the micro-arc to which it appears to give rise in certain conditions. At the same time, work in this field is enlarging our knowledge of the properties of metals at very high temperatures.

Another important conclusion can be drawn from this most interesting and worth-while symposium. In the conference of 1952 it was not clear that the engineer concerned with the operation of contacts, and the physicist concerned with fundamental processes, were attacking the problem together; at the present conference there appeared to be far closer liaison between the physicist and engineer, and, further, it was apparent that the designer now fully appreciates methods of approach depending on investigation in controlled conditions of, for example, ambient atmosphere and surface state.

Dr. J. Topping, principal of the Brunel College of Technology, who welcomed and opened the conference, is to be congratulated on the excellent arrangements.

GAS CHROMATOGRAPHY

THE Gas Chromatography Discussion Group held its third annual general meeting on April 21 at the University of Birmingham. Membership had risen by 75 during the preceding year to 346, including 94 from 18 countries other than Great Britain.

Highlights for the year had been the publication of the first two volumes of *Gas Chromatography Abstracts*, and the very successful third international symposium at Edinburgh the previous June which had attracted more than five hundred delegates from twenty countries. The *Proceedings* had been published in a 466-page volume before the end of the year.

The group is planning another informal symposium in the autumn, and arrangements for the fourth international symposium, this time in Hamburg during June 13–16, 1962, are already well advanced.

The Retention Data Sub-Committee reported that very little data had been submitted to them, and after considerable discussion agreed to consider the usefulness of relative retention data, which require less rigorous control of conditions and would probably be more readily available than the absolute data they had been seeking.

The scientific section of the meeting opened with a welcome by Prof. R. C. Robb.

The first paper was presented by Mr. M. B. Evans on the relation between the retention volumes of unsymmetrical compounds and cognate symmetrical ones. The work has since been published in the *Journal of Chromatography*[1].

Mr. C. E. Roland Jones discussed technical details in the examination of pyrolysis products, describing a micro-apparatus for use with the Pye argon chromatograph. He illustrated its use in the identification of plastics, especially those which were not amenable to identification by infra-red spectroscopy.

Dr. R. P. W. Scott discussed the effect of temperature on resolution both theoretically and in the light of experimental results. He showed that for any required separation there was an optimum temperature for a given film thickness and this was more marked with thick films of stationary phase than with thin ones; conversely there was an optimum thickness for a given temperature and an optimum combination of both for minimum analysis time.

Dr. I. Halasz read a paper entitled "Quantitative Analysis of Hydrocarbons with Capillary Columns and Flame Ionization Detectors". He had investigated thoroughly a large number of factors affecting quantitative accuracy, and designed a stream splitter which apparently eliminated the uncertainties of previous models since the scores of tabulated results which he produced showed a consistent accuracy of about 1 per cent.

In the discussion which followed, Dr. Kovats produced some quantitative results from 2 μl. of rose oil on an unusually wide capillary column used in conjunction with a tungsten filament katharometer. Efficiencies of 40,000–100,000 theoretical plates had been obtained from such columns.

The final paper by J. G. A. Hölscher of the University of Eindhoven was presented by Dr. M. Van Swaay. He was able to show that ionization in argon detectors could be caused by photons from a pulse discharge. Such a discharge caused a current to flow between two electrodes in a mixture of argon and a hydrocarbon, with a time lag characteristic of the velocity of photons rather than metastables, ions from the discharge being screened off by a series of grids.

S. J. HAWKES

[1] *J. Chromatog.*, **5**, 300 (1961).

TELEVISION AND FILM TECHNIQUES

A CONVENTION on television and film techniques, sponsored jointly by the British Kinematograph Society and the Television Society, was held at the Institution of Electrical Engineers during April 20–21.

Sir Harold Bishop, director of engineering of the British Broadcasting Corporation and president of the Television Society, opened the Convention with an address on the topical problems of television in the United Kingdom. He said that the B.B.C. supported the report of the Television Advisory Committee and that it was convinced of the long-term advantages which would result from the use of 625-line standards in the ultra-high-frequency bands IV and V (470 Mc./s.–960 Mc./s.). In particular, line visibility was notably less than with our present 405-line standards and the introduction of larger screens would aggravate the 'lininess' of the present images. Programme interchange with European countries, all of which except France had adopted the 625-line standard, would also be facilitated. Sir Harold also spoke of the B.B.C.'s wish to start a limited service of colour television compatible with the present 405-line service in band I.

Mr. J. Roizen gave a lecture on "The Use of Videotape for Colour Television Recording". He described the various methods that the Ampex Co. in California had investigated with the object of achieving satisfactory magnetic-tape recording of colour television signals. The composite colour video signal contains a subcarrier which is, in the American National Television System Committee system, amplitude-modulated with chrominance signals in phase quadrature. The frequency of this subcarrier is 3·59 Mc./s. and 1 cycle, or 360° of it, occupies a time duration of 0·28 μsec. The phase of the vector representing the chrominance signal carries the information from which the colour being transmitted is obtained and it has been found by experiment that errors of the order of 5° can be detected by a skilled viewer. A 5° error phase can therefore arise from a time variation or error of 4 nanosec. (10^{-9} sec.). In the recording of television signals on film (telerecording), the complete television image is exposed to the film, but in magnetic-tape recording the signal wave-form is recorded as a function of time or distance across, and along, the tape, the synchronizing pulses also being included. It is apparent that any non-uniformity of relative velocity between tape and 'head wheel', in the periphery of which four recording heads are embedded, will give rise to a timing error which will result in a change of the resulting colour. One line of investigation consisted, therefore, of an attempt to stabilize the relative velocity between tape and 'head wheel' to a much greater precision than had been required for the recording of monochrome (black-and-white) television. The servo-mechanism normally used employs a 240 c./s. electric signal derived optically from black-and-white patches on the 'head wheel', but a more accurate feedback signal was needed so the frequency was raised to more than a hundred kilocycles per sec. Even this was scarcely adequate, and another line of investigation led to the correction of signal-timing errors by means of a delay line having a controlled variation of delay. The difference in phase between the synchronizing signal derived from the video wave-form of the outgoing 'playback' television signal and a source of stable synchronizing signals is used to control the capacitance of a silicon diode forming part of the capacitance of the delay line. The outgoing video signal is passed through the delay line, and the delay is varied in such a manner as to compensate for the timing errors in the signal. The compensation is such that quite satisfactory results are now obtained: the timing error accumulated during the interval between successive colour synchronizing signals (a line-scan period) presumably being not greater than a few nanosec. The scheme described is known as 'Super-Amtec'.

Mr. B. J. Davies described a rapid-processing machine for 16-mm. film. The increasing use of magnetic-tape recording for television, or 'videotaping' as it is now termed, has caused the technical side of the film industry to consider means of accelerating the developing of film to the point at which it offers an attractive alternative method of making permanent records of television programmes, despite the fact that the advent of 'videotape' has resulted in an increase in the use of film in the television industry. The Kodak Co. has developed this machine around a very rapid processing cycle, the duration being about 60 sec. and the film velocity 38 ft./min. The method is called viscous-layer processing and is a departure from the liquid-bath methods previously used. The developer and fixer are applied to the photographic emulsion by means of special rollers over which the film is passed.

Messrs. Polonsky, Cassagne and Sauvanet described "Recent Progress in the SECAM Frequency Modulation Colour Television System". This system of colour television, the idea of M. Henri de France, has been developed by the Compagnie Française de Télévision, and has been improved over the years by the authors and M. Chaste who, with M. Cassagne, delivered a paper on the subject before the Institution of Electrical Engineers in April 1960. As in the American National Television System Committee's method, the colour information is transmitted by means of a modulated subcarrier but, instead of amplitude modulation being used, the subcarrier is frequency-modulated. Furthermore, unlike the Committee system wherein both the amplitude and the phase of the amplitude-modulated subcarrier are used simultaneously, the one representing saturation and the other hue, in the SECAM system the frequency-modulated subcarrier represents only one quantity at a time (television line by television line). This subcarrier is thus frequency-modulated alternately, line by line, by one of two colour-difference signals (for example, red intensity minus luminance and, afterwards, blue intensity minus luminance). This method of transmitted colour information renders the transmitted signal more 'rugged' and resistant to the various electrical and propagation hazards likely to be encountered. It is claimed that colour receivers based on this system are simpler to align in the factory, easier to service and more stable, as well as being more suitable for an unskilled viewer to operate. The receiver requires an expensive delay

line in order to compensate for the non-simultaneous transmission of colour signals, and there is a theoretical loss of vertical colour resolution of two to one as compared with National Television System Committee, but the authors state that the Committee's system contains several times more vertical colour resolution than is required, and it must be said that the excellent demonstration given by the authors, with assistance from the Hirst Research Centre of the General Electric Co., the General Post Office and the B.B.C., showed no apparent lack of vertical resolution. It was suggested that, from the technical and picture quality point of view, there was little to choose between the SECAM and the National Television System Committee systems.

Dr. W. E. Glenn described a thermoplastic recorder for television and similar signals. The device, developed in the General Electric Research Laboratories in Schenectady, bears a fundamental resemblance to the Eidophor, which will be mentioned later. Brighter pictures than those from a cathode-ray tube could be obtained if the image were stored for display and then illuminated by a separate source of light, such as an arc. Photographic recording (telerecording) is a good example since, in reproduction, a film projector may be used, although many applications require re-televising of the storage medium. In Dr. Glenn's apparatus, which consists of an evacuated enclosure, an electron beam, appropriately modulated with a television signal and deflected in the usual manner of scanning impinges on a thin film of low-melting-point thermoplastic on which a charge image is thus placed. Beneath the top film is another of a transparent conducting material and beneath this is a transparent high-melting-point tape. The conducting layer acts as one plate of a condenser, the other being the charge image itself. By melting and then freezing the top layer, the charge image is replaced by the same image impressed into the thermoplastic by electrostatic force in the form of hill-and-dale deformations. The film or tape now has a permanent record on it and may be stored for subsequent play-back. For this purpose a modified schlieren optical system and a light source are required, although, for editing purposes, the actual image can be made visible on the film. The entire process of melting and freezing the thermoplastic takes a few milliseconds, and the ultimate resolution is limited by the wave-length of the light used for projecting (200 television lines per mm. is a practical figure). For colour images, a phase-diffraction-grating method may be used and a special optical system is required for projection. The author projected some thermoplastic film through a suitably modified projector.

Prof. E. Baumann described "Recent Developments on the Eidophor Large Screen Projector". The idea, conceived by Prof. Fischer in 1939 and afterwards developed with Dr. Thiemann, Prof. Baumann and others at the Zurich Technische Hochschule and, later, by Eidophor, Ltd., relies on the light-valve principle described earlier. In an evacuated enclosure, an electron beam, suitably modulated with a television signal and scanned in the usual manner, 'writes' a charge image on a thin film of oil on the conducting surface of a concave mirror. The viscosity of the oil is sufficiently low to allow the electrostatic forces between the charge image and the mirror surface to deform the oil into hill-and-dale irregularities. The mirror is in the light path of a schlieren optical system, and the deformations of the oil, acting as the reflecting surface, are revealed as optical images on a large projection screen. Prof. Baumann demonstrated the Eidophor by receiving, from a B.B.C. studio, a 405-line film transmission which, after passage through the Eidophor, was seen on the large screen in the lecture theatre. Although the film was not particularly bright, the possibilities of the system were quite apparent.

Mr. Grimshaw of the Kodak Co. read a paper by Messrs. Veal and Richey of Eastman Kodak Research Laboratories, Rochester, U.S.A. The paper, "Technical Requirements of Systems and Film for Colour Television", dealt with the difficulties of reproducing colour film on colour television. In particular, the contrast-range normally encountered in colour film is too high for colour television, resulting in loss of luminance and colour information in dark parts of the viewed image. Whereas a contrast-range of 100 : 1 is not rare in film, colour television is at its best within a range of about 20 : 1. This is due to many causes, but it is not difficult to see that, since the optical projection of film in the cinema (or home) relies on the light-valve principle, in which a source of light illuminates a screen after multiplication of the light intensity by the transmission factor of the film, the contrast-range of projected film may be limited only by flare and diffusion in the projector and on the screen, provided that the ambient illumination of the screen is zero. The fact that the reproduction of colour by photographic film is a negative-colour process, whereas its reproduction by television is a positive-colour process, also makes the colour televising of colour film rather more difficult. The paper presented graphs which revealed that greater horizontal resolution could be obtained from a three-Vidicon film scanner than from a flying-spot film scanner employing three photomultiplier cells. This came as a surprise to some members of the audience, who wondered whether American experience with flying-spot scanners had, perhaps, been less extensive than European.

Messrs. A. R. Stanley and J. Treays read a paper entitled "Colour Television Engineering: Studio Problems and Techniques". They gave a short historical account of the experimental colour transmissions radiated by the B.B.C. and went on to discuss a number of matters connected with studio programmes in colour. Experience showed that it is preferable for each picture-originating source to have its own coder so that the primary-colour signals are not sent round the studios. They found that the composite signal, that is, the luminance signal added to the modulated subcarrier, was more 'rugged' and suitable for the various processes which occur in a television studio, such as cutting, mixing and fading. It was interesting to note that during a slow mix from one composite colour signal to another, during which the two signals are added, the resulting colours were quite satisfactory and gave the impression of two colour pictures being superimposed. Presumably because a colour picture contains more information, it was found that individual shots could last longer than in the case of a monochrome programme, although the compatible black-and-white programme viewer must not be forgotten. The performers' make-up presented some novel problems: it seems that the chemical composition of perspiration varies from individual to individual and the colour of make-up can vary throughout a day's rehearsals and performance. Coloured performers

require less make-up and are, therefore, easier to deal with than white people. In order to align and set up the cameras, these were presented with a set of Munsell colour chips illuminated by the normal studio lighting and the images on the picture monitors in the control room were compared with a similar set of Munsell chips illuminated with illuminant *C*, which has the chromaticity of the 'white' standard for the National Television System Committee colour television. When a programme involves film inserts, great care has to be taken to ensure a colour match between similar scenes which may be viewed in succession from a colour-television camera and from a colour-film scanner, or telecine machine. Although the necessarily low contrast required for the colour transmission seemed to be quite satisfactory for the compatible monochrome viewer there was, at times, a subtle change of mood in that the dark colours which were required for the colour viewer made the compatible black-and-white picture rather sombre. During the lecture, some very fine colour slides were projected, showing studio scenes for colour programmes.

Messrs. A. R. Stanley and S. N. Watson introduced "Colour Television Engineering: Equipment Problems and Techniques". The authors discussed five characteristics of colour television which gave least satisfaction to viewers during the B.B.C. colour field-trials mentioned in the historical survey of the previous paper. It had been clearly demonstrated that the colour cameras were the weakest link in the chain. The paper dealt with a number of matters which affect the correct reproduction of colour scenes. For example, no effort is made to ensure negative lobes in the spectral response characteristics of the colour analysis filters in the cameras, although it is possible to achieve an approximation to negative-lobed characteristics despite the impossibility of using 'negative light'. The 'taking gamma' of the cameras is important, as are the errors due to shading (or spurious) signals in the image orthicon tubes used in the cameras. The latter may cause errors of hue, particularly in low-luminance patches of the scene. Since the phase of the modulated colour subcarrier determines the reproduced hue, any departure from linearity of the phase/frequency characteristic of any part of a transmission network in the region close to the frequency of the subcarrier (2·66 Mc./s. in the case of the National Television System Committee system adapted to 405-line standards) causes errors of hue. In particular, if the transmission system suffers from a non-linear effect which causes a change of phase to occur in sympathy with a change of signal-level (in the composite video signal the luminance signal and the chrominance or modulated subcarrier signal are added) a change of hue and brightness will result. The possible existence of this phenomenon places a rather stringent requirement on the linearity of television equipment such as studio broadcast apparatus, and radio links. An excellent demonstration followed the lecture. Colour film and slides originating in a B.B.C. studio were transmitted by Post Office equipment to the lecture theatre of the Institution of Electrical Engineers and the received images were projected on to the large screen by a Marconi's Wireless Telegraph Co.'s three-tube Schmidt projector. The registration of the three primary-colour images was very good indeed. The effect on hue of a 10° change of subcarrier phase was shown and also the deterioration in picture quality to be expected from the use of two transmission links in series. Both deteriorations were slight. The technique of using a low-pass filter to attenuate all Fourier components (and noise) of the luminance signal, which would otherwise occupy the frequency band set aside for the chrominance signal (which shares an upper part of the full luminance channel) and the subsequent employment of a non-linear device ('crispener') to reconstitute artificially an impression of sharpness was also successfully demonstrated. An electronic masking unit showed how an improvement can be made to the properties of colour film for colour-television purposes.

R. D. A. Maurice

STUDY OF DEFECTS IN PORPHYRIN METABOLISM BY MEANS OF ISOTOPES

THE Biology Division of the French Atomic Energy Commission held, during September 1960, a colloquium at Saclay on the use of tracers in the study of diseases of porphyrin metabolism. Participants from Europe and the United States enjoyed three days of intense discussion as guests of the Atomic Energy Commission and the Ministry of National Education. The topics debated ranged over a wide field; full proceedings of the conference will be published in due course.

In the opening address, Prof. A. Bénard reviewed our present knowledge of porphyrin biosynthesis and of the disturbances giving rise to the different clinical forms of porphyria. It was his view that such diseases were variants of a single fundamental abnormality. Symptoms were due not to the porphyrins themselves but to associated metabolic disturbances such as interference with the synthesis of purines. He concluded an impressive survey by reference to recent therapeutic measures which have shown some promise in the treatment of acute porphyria, namely, administration of 2 : 3-dimercapto-propanol, ethylenediaminetetraacetic acid or adenosine monophosphate.

The genetic aspect of the porphyrias was then dealt with. It was pointed out that the several hundred South African cases of 'porphyria variegata', all being descended from a single pair of Dutch settlers, necessarily represent manifestations of the same genetic abnormality or group of abnormalities found in the progenitors and might well, therefore, display a characteristic pattern. A fascinating account of the recently discovered 'Turkish porphyria' was given by Dr. R. Schmid. It is an acquired porphyria due to consumption of wheat containing hexachlorobenzene. Several thousand human cases have occurred and the disease has also been reproduced experimentally in animals. Topics further discussed during the first day's sessions were the symptomatology of acute intermittent porphyria and its causation, and also the difficulties attending the interpretation of investigations made with isotopic tracers on such patients.

While it is generally felt that the excessive excretion of porphobilinogen and δ-aminolævulic acid in acute hepatic porphyria is due to over-production of these materials, the exact biochemical mechanism leading to such over-stimulation of the porphyrin pathway is still in doubt. Experiments designed to test the possibility of restricted conversion of glycine into serine were inconclusive. A hint as to the means by which δ-aminolævulic acid production is normally regulated may be forthcoming from the experiments described by Shemin who showed, in one system studied, that δ-aminolævulic acid is itself an inhibitor of the enzyme producing it. This points to the possibility of a negative feed-back control operating in the normal cell. The combination of administration of porphyrinogenic drugs with pantothenate deficiency promises to throw further light on the development of the nervous symptoms in acute porphyria. It has been generally assumed, since the self-experiment of Meyer-Betz, that photosensitization in the cutaneous porphyrias is actually caused by the porphyrins themselves. Direct evidence was lacking, however, until quantitative measurements were made by Magnus and collaborators on patients with the use of a powerful monochromator. This technique and the results it afforded were described and exemplified by the case of a man with sun-burn type photosensitivity who, nevertheless, showed highest cutaneous sensitivity in the Soret band region of the spectrum. Further investigation showed that his red cells and faeces did, in fact, contain abnormally large quantities of porphyrins.

The increase in urinary excretion of porphyrin which accompanies lead intoxication has aroused the interest of biochemists for many years, but is as yet little understood. New light may be thrown on this problem by the finding of Gajdos and his collaborators that lead ions interfere with the passage of iron through the membrane of the developing red cell, the stroma, under these conditions, retaining iron rather firmly.

The biochemical mechanism of incorporation of iron into protoporphyrin and the part played by 'bound' forms of these reactants, the biosynthesis of porphyrins by human leucocytes and the metabolism of hæmoglobin within the red cell were next considered. It would appear from the work of Schapira and his co-workers that the hæmoglobin molecule within the erythrocyte is not metabolically inert, but that progressive structural alterations occur with the course of time. The effects of radiation on the synthesis of hæmoglobin in the bone marrow, and the results of a great deal of work on the relation of porphyrin structure to X-ray sensitivity, were also reported.

At the close of the meeting, Prof. C. Rimington endeavoured to lay before participants an appraisal of the most significant conclusions and to point to the fields from which the next major advances towards an understanding of normal and pathological porphyrin metabolism might be expected to come. He took the opportunity of thanking the organizers and the two bodies sponsoring the colloquium for their excellent work on behalf of porphyrin biochemistry and for their generous hospitality. This meeting will be long remembered with gratitude and pleasure by those who were gathered together in the stimulating atmosphere of Saclay.

C. Rimington

CONSERVATION OF BRITISH NATIONAL PARKS

In its recent eleventh annual report the National Parks Commission referred briefly to the question of afforestation in the National Parks, especially on Dartmoor and Exmoor, and also to its disappointment at the delay in amending the Act, particularly with regard to financial resources. Both these aspects have since been the subject of short adjournment debates in the House of Commons. In the first of these, on March 29, Mr. E. du Cann raised the question of afforestation, particularly in the Dartmoor and Exmoor National Parks. While supporting the voluntary agreement recently reached between the Timber Growers' Organization, the Country Landowners' Association, the Forestry Commission and the National Parks Commission regarding afforestation in the National Parks, Mr. du Cann questioned whether a voluntary agreement would be sufficiently effective, as it did not include all those concerned with afforestation in such areas.

In his reply, the Parliamentary Secretary to the Ministry of Housing and Local Government, Sir Keith Joseph, agreed that it was important to give the new scheme a fair trial. He thought that there was no reason to fear that landowners in the areas concerned, who were not members of the Association, would not, as individuals, comply with such agreements and, in reply to a specific question about trees on High House Moor, Dartmoor, said that discussions were still proceeding between the proposed developers and the authorities. On this specific issue it should be noted that considerable uneasiness still exists that the National Parks Commission will not be supported. The parties to the agreement were not despondent as to the prospects that the agreement would succeed, and Sir Keith Joseph appeared to have substantial grounds for his confidence that the spirit of co-operation already demonstrated by the production of this voluntary agreement, and the way it had been received and implemented indicated that, with common sense, it should be possible to reconcile the claims of forestry and the National Parks and the rights of landowners.

Nevertheless, Sir Keith recognized that failure of the scheme would create a new situation and this would have to be faced. Meanwhile, he said, the Minister wished to give the scheme a fair trial and he made it clear that he also wished that all concerned, whether members of the particular organizations or not, should participate in this voluntary consultation at all times. The Minister and the National Parks Commission would keep progress under careful review.

On the wider issue raised in the debate on March 30, progress also may be regarded as largely a matter of co-operation and common sense, but on the part of the Government common sense implies providing the financial means to the end enacted. The root of the difficulties encountered in the development of

the National Parks lies in the failure of the Government to provide, under the National Parks and Access to the Countryside Act of 1947, the finance required to make the provisions of the Act effective. Under that Act the responsibility for the National Parks was placed within the planning system set up by the Town and Country Planning Act of 1947 instead of the national system envisaged by the Hobhouse Committee. The counties provide two-thirds of the Committee members and almost all the funds, although some of these counties are among the poorest in the country.

Nevertheless, the system has worked surprisingly well, though it is obviously unfair to expect local authorities to take a national point of view, and invariably set the national interest before local interests, particularly at heavy cost to the ratepayers who elect them. The advantages of close association with local interests are such, however, that in view of this experience, it seems highly probable that, given quite moderate Government support, sufficient, for example, to ensure the provision of adequate planning staff and a reasonable contribution to the capital costs of positive projects of development, the existing system could well be continued with success. Much could be done if the National Parks Commission had an annual sum of even as little as £100,000, in place of the present £20,000 (with some £5,000 in Exchequer grants to the National Parks), which it could use at its discretion, either in helping the weaker authorities to strengthen their planning staffs, or in assisting projects which, at present, the park planning authorities hesitate to undertake because of their fear to place excessive burdens on local ratepayers for the benefit of outsiders.

Such a system admittedly is pragmatic rather than the ideal national system, in which national purposes and projects are financed directly from national funds, as Mr. F. H. Hayman advocated on March 30. Admittedly, the development and preservation of the National Parks is often too dependent on the finance committee of the county councils concerned, as Mr. Hayman pointed out ; but to transfer the whole cost of the National Parks to national funds is not the only way of overcoming the difficulty, and if such a transfer lost local interest in, and support for, the National Parks the price might well lead to local misunderstanding and opposition. Mr. Hayman did not, however, appear to advocate quite such a drastic step though he made it clear enough that local resources and prejudices should not determine the objectives and purposes of a national undertaking.

In replying on this debate, Sir Keith Joseph asked for specific examples of projects which were now being frustrated by lack of funds, but claimed that direct Parliamentary grant, and not discretionary payment, was the appropriate way to finance public schemes. He confirmed that the Minister would look at all proposals made to him for amending the Act and said that he was at present seeking more information from the National Parks and the National Parks Commission to assist in this review. Sir Keith was emphatic that there was much more which could be done by the individual Park Committees which would receive Exchequer aid up to 75 per cent, but he thought the time might well have come to extend the legislative framework in some ways. Nevertheless, he did not think that finance was the only answer. Vigilance, effective administration and an imaginative approach must also play an important part, and probably the main value of both debates lies in the extent to which they demonstrate the need for public co-operation and understanding, and for such unceasing vigilance if the purposes of other Parks or Nature Reserves are to be served.

The whole subject was further discussed in the House of Lords on April 19 on a motion of Lord Silkin, who again stressed the importance of adequate financial provision. Lord Feversham also pointed out that existing provisions were completely inadequate, either to prevent or to control fires on heaths and moors, and Lord Dalton, who agreed as to the need for adequate financial provision, also pressed the claims of the long-distance footpaths. Lord Chorley specifically suggested that the National Parks Commission should have an annual sum of £150,000 at its disposition, and like most other speakers was critical both of the Electricity Authorities and of afforestation, though tribute was freely paid to the sympathetic attitude of the Forestry Commission and its present chairman. Earl Jellicoe, who replied on the debate for the Government, added little to what had been said in the Commons by Sir Keith Joseph, but referred particularly to Lord Feversham's suggestion of a direct Treasury grant to the National Parks Commission.

THE RESEARCH COUNCIL OF ALBERTA

THE forty-first annual report of the Research Council of Alberta covers the year 1960*, and includes a list of publications for 1956–60, and lists of members of Advisory and Technical Advisory Committees and of the staff of the Research Council. The Petroleum Division of the Fuels Branch has largely completed its work on the movement of oil in the presence of water in a pipe-line, and studies on capsule pipe-line transportation indicate that the presence of capsules in a flowing stream does not significantly alter pressure gradients, nor does the moving core appreciably distort the flow in the annulus. The capsule velocity appears to depend directly on capsule length and inversely on capsule diameter. The Division has also completed the first major phase in developing a generalized mechanism for the control of composition and accumulation of crude oils and natural gases in sedimentary basins, and the light paraffinic oils, which are usually found in positions corresponding to the areas of maximum depth of sedimentary basins, appear to owe their paraffinic constitution to the extensive action of oxidation and microbiological attack, both of which tend to destroy the less-resistant components of the developing crude oil. With the Coal Division the Petroleum Division is studying the transport of mixtures of pulverized coal and oil, while the Coal Division has also studied the combustion of pulverized fuel, the crystal structure

* Research Council of Alberta. Forty-first Annual Report, 1960. Pp. v+55. (Report No. 80.) (Edmonton: Research Council of Alberta, 1961).

and magnetic properties of coal chars, the plastic properties of Alberta coking coals and coal blends. Work on the mechanisms of coal pyrolysis and carbon formation is expected to bear directly on carbon production from low- and medium-rank coals, and physico-chemical investigations on humic acids from coal have shown that simple coupling reactions can convert humic acids into water-soluble materials without otherwise altering their chemical properties, and that humic acids can be made to yield five-membered cyclic anhydrides.

The Natural Gas Division has been engaged largely in the separation of gases by selective adsorption on porous solids and with catalytic reactions in the adsorbed state, particularly the catalytic conversion of *cyclo*propane to propylene on crystalline alumino-silicates. The Groundwater Division has provided information which assisted in meeting several serious water shortages, while the programme of the Geology Division included a study of the fossil content, distribution and physical make-up of Cretaceous rocks, the study of iron deposits and examination of a gypsum deposit at Mount Head. The reconnaissance soil survey of the Hines Creek map sheet was completed, as well as an exploratory soil-survey by helicopter of some 10 million acres in the north-western part of the Province, while the Soils Division has also co-operated in work on the classification of forest sites and the irrigation of Solonetzic soils. The basic cloud-physics programme, with special reference to hail, included establishment of an enlarged meso-barograph network covering 10,000 sq. miles, upper wind observations stations at Penhold, Rimbey and Rocky Mountain House, and an expanded hailstone collection network. Synoptic investigations on hail now permit some differentiation of storms as related to certain areas to low-level convergence and moving cold-front activity.

ERADICATION OF MALARIA

ALTHOUGH progress towards world-wide malaria eradication has, in general, been satisfactory, there are some malaria eradication programmes that have failed to develop as speedily as they could. A report of the World Health Organization's Expert Committee on Malaria is mainly concerned with the reasons for these failures, and with methods of increasing the efficiency of eradication programmes*.

The technical, operational and administrative causes of failure are analysed in detail, and it is emphasized that success depends not only on careful planning and meticulous execution of the programme but also on the full support of the national authorities at every stage. This must be ensured at the outset by a signed undertaking from the Government.

The criteria given in the Committee's seventh report for discontinuing spraying operations and starting the consolidation phase are amplified and a fresh criterion added, namely, that surveillance should be fully established and adequate. The measures undertaken should include the passive as well as the active detection of cases, this being the only way to ensure that all areas are reached and that observations are continuous. With the view of reducing the costs of the consolidation phase without sacrificing efficiency, the report recommends that the World Health Organization should study the costs by heads of expenditure in as many countries as possible, and should encourage the detailed analysis of costs both by activity and by heads of expenditure in selected representative countries.

The report reaffirms that eradication may be considered to have been achieved "when an adequate surveillance mechanism has not discovered any evidence of transmission or residual endemicity, despite careful search, during three consecutive years". The criteria of eradication given in the sixth report of the Expert Committee on Malaria are re-examined; while the basic principles remain unchanged, the criteria are re-defined and expanded in order to cover the needs of special situations that have been met in practice. With the aim of establishing an official register of areas where eradication has been achieved, recommendations are given on the methodology of inspection and certification.

In countries where the administrative structure and the health services are still in the developmental stage, a "pre-eradication programme" may be necessary to create suitable conditions for the success of malaria eradication. An outline of such a programme is given, and it is suggested that an international team should be provided to advise the Government and, if necessary, to carry out the initial stages of the programme.

Health education forms an essential part of a malaria eradication programme; it must reach all levels of the population from the outset of the campaign and be continued throughout the consolidation and maintenance phases, in order to ensure continued co-operation of the public at a time when interest in malaria will have begun to wane. The report advocates that provision should be made for a special staff to run health education programmes under the malaria eradication programme.

The establishment of a standard terminology for use in evaluation and surveillance was considered by the Committee to be highly desirable, and it was recommended that the World Health Organization set up a drafting Committee to undertake this task.

The report directs attention to the value of chemotherapy in the attack phase of eradication programmes as well as in the later stages. The 4-aminoquinolines remain the most effective drugs and no significant changes are recommended in the regimen for radical cure. The use of salt medicated with chloroquine shows promise. Research is needed on the improved use of available drugs and to discover compounds with an improved action against malaria parasites.

It is believed that, in some countries, a reduction in the standard dosage of DDT (1 gm./sq. m.) used in spraying might be possible, but no such reduction should be made until appropriate field trials have provided unequivocal evidence that this would not jeopardize the success of the eradication programme.

Finally, the report considers the relation of simian to human malaria, particularly the recent experimental transmission of malaria from the lower monkeys to man. It is concluded that the practical importance of a simian reservoir of malaria is likely to be small.

* World Health Organization. Technical Report Series, No. 205. Expert Committee on Malaria—Eighth Report. Pp. 50. 2 Swiss francs; 3s. 6d.; 0.60 dollar. (Geneva: World Health Organization; London: H.M.S.O., 1961.)

A READING MACHINE FOR THE BLIND

By M. P. BEDDOES, E. BELYEA and Prof. W. C. GIBSON

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WE have investigated possible methods by which a machine can help blind persons to read from the printed page. This article describes work done on the problems of recognizing the alphabet letters, coding the output, and placing a hand-held pick-up probe accurately on the page.

The first notable reading machine was called the optophone by its inventor Dr. E. E. Fournier d'Albe[1,2], and in the early 'twenties a speed of 25 words a minute was claimed.

A devoted but small band of people have laboured with it since then with results, quoted recently in the Press[3], of up to 60 words a minute. This is not impressive considering the vast amount of experience which has been gained over the years, and it indicates two defects of the optophone principle: one is that the code sounds are difficult to learn; the other is that the fastest rate is well below that of normal reading speeds.

An American version[4] of the optophone which employs up-to-date engineering techniques has been disappointing also. Tests in progress since 1957 have established reading rates, when tape-recordings of the code-sounds are presented to subjects, of about 30 words a minute; but when a hand-held pick-up probe is used, 8 words a minute seems to be the fastest rate for experienced operators. The differences in the rates of the two versions (60 down to 8 words a minute) lie chiefly in the fact that the English machine uses a mechanical device scanning along the line to be read whereas the American one uses a manually held pick-up probe. The latter has advantages as regards cost, reliability and convenience to the user which are, at present, outweighed by its poor performance.

The optophone converts material from the page, a letter at a time, almost directly into electrical signals. For this reason it has been called[5] a 'direct translation' machine. Our work is with a 'letter-recognition' machine, so called because it first identifies (or 'recognizes') a letter and then triggers the appropriate code sound. With this type of machine there is a wide choice of audible codes making possible psychological advantages in learning and increased speed. Many workers in recent years have favoured the 'letter recognition' approach[7–11] because it permits the problems of identifying letters and of designing a suitable output code to be dealt with independently of one another.

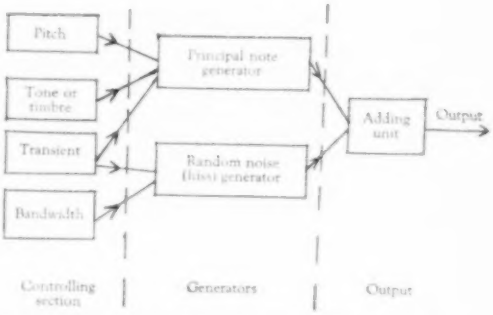

Fig. 2. Block diagram illustrating the generation of the sounds for the blind readers' code

The problem of recognizing standard typewritten print was investigated. Transparencies were made from impressions on ordinary bond paper of upper-case and lower-case alphabet letters from a portable typewriter. These slides were scanned by a flying-spot cathode-ray tube (Fig. 1). Sawtooth scanning was employed: vertical rate = 3,300 c.p.s.; horizontal rate = 80 c.p.s. Output from a photo-multiplier was processed by an R–C integrator with a time-constant of 11 m.sec. The scanning rates are not critical provided that this time constant is short compared with the period of the horizontal scanning (= 125 m.sec.) and long compared with that of the vertical scanning (= 0·3 m.sec.).

The operation of the apparatus is as follows. The output voltage, V_o, was large when scanning a long vertical line of appreciable width; such a line, for example, is the principal part of the letter I and is known as a 'riser'. Risers in letters b, d, f, h, etc., were easily spotted from the wave-form of V_o. A single horizontal line in letters such as n and u, etc., gave rise to a small value of V_o.

In identifying a letter, the apparatus of Fig. 1 may be used. The following sequence of tests on the wave-form V_o was found necessary: (*a*) measurement of the height of the first maximum (results in Table 1: accuracy of ± 0·05 in 3 or ± 1·7 per cent is necessary); (*b*) measurement of the minimum following the above maximum; (*c*) a count of the number of maxima (used with letters such as m, w, M and W), with the scanning raster rotated through right angles; (*d*) measurement of the maximum; (*e*) measurement of the minimum between any adjacent maxima. Analogue and digital techniques are both used, and all letters can be decoded. The number of tests required to identify a letter varies, but the greatest number is four.

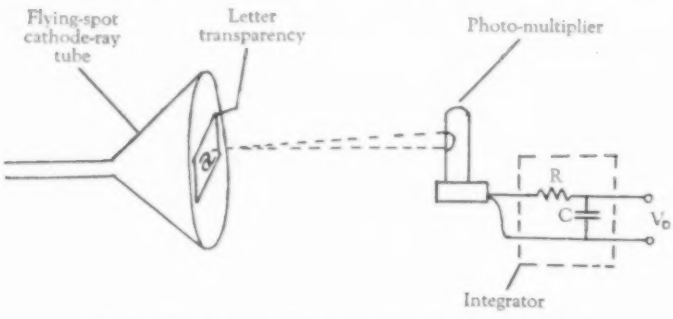

Fig. 1. Apparatus for investigating properties of letter recognition

Table 1. Classification of Letters according to Height of First Maximum of F_2

Height	1·0	1·1	1·2	1·3	1·4	1·5	1·6	1·7	1·8	1·9	2·0	2·1	2·2	2·3	2·4	2·5	2·6	2·7	2·8	2·9	3·0
Letter			dj			xy	cs	oa	cuw	gmz	v	n	k	f	rbth	i	p			q	
Letter									CGO	SX	V	UZ	AMN		RY	HJTW	BDK	FQ	E	LP	I

In order to arrive at the best coding for the alphabet letter detected by the above procedure, we conducted experiments with various proposed audible codes of a semi-musical nature. Each alphabet letter is represented by a single sound (as opposed to the many in Morse). Such a sound is the result of combining the components listed below.

(*a*) 'Pitch'—four frequencies (corresponding to doh, ray, fah and sol of the sol-fah notation). (*b*) 'Timbre'—two wave-forms (sine-wave or rectangular wave). The above are produced in the 'principal note generator' (Fig. 2). (*c*) 'Hiss'—broadband noise from a separate generator is filtered through one of three bands in the audio spectrum. (*d*) 'Transient'—with or without a click at the commencement of the sound. Sixty-three distinct sounds can be made. The above list represents the best compromise obtained so far as judged by the following experiments.

Experiments were made to determine whether or not the components could be perceived either singly or in the presence of others. A pair of sounds each 0·1 sec. long and separated by 0·1 sec. silence was conveyed by a loudspeaker to a subject who was asked to judge if the pair was made up of the same sounds or different ones. About two hundred such tests, each separated by 3 sec., were presented to up to seventy-six subjects at a time. Errors with the final code (above) were less than 10 per cent.

The choice of components was made so that clear patterns were perceptible when the sounds were presented rapidly. The following word experiments indicate that such is the case.

Eleven three-letter words were chosen. Each was coded to occupy 0·7 sec., and they were presented in six random sequences to seven blind persons. Ages varied from 15 to 52 years; average age was 33. The code version of the word was followed by a 10-sec. silence; this was followed by the spoken word, and, finally, by the code-version again. Words were always presented in this order. In the first sequence, words were heard for the first time, but nothing was required from the subjects. In the second sequence and those following, the subjects were asked to write in Braille the appropriate word in the 10-sec. pause. Their 'guess' was confirmed or corrected by the subsequent voice-code cycle. Results are given in Table 2; no difficulty was found in decoding meaningful sentences made of strings of these words.

Further word experiments using the same material with some additions were made with thirty-seven sighted university undergraduates in psychology. Results are not as good as those for the blind group (cf. Table 2 with Table 3), but are still considered to be acceptable. Poor motivation probably accounts for the slower learning-rate.

Table 2

Sequence	2	3	4	5	6	7
Correct (per cent)	65	60	82	82	80	80

Table 3

Sequence	2	3	4	5	6	7	8	9	10	11	12
Correct (per cent)	17	23	33	42	44	48	53	54	59	62	63

A machine has been constructed with a hand-held probe for reading a very special type of print—printed Braille. This machine is being used to investigate the problem of placing the probe accurately on the page. A feature is its simplicity. Six miniature photocells are used to read from the Braille character; three cells are used to identify position; eighteen transistors and nine relays are required for reading purposes; only six transistors are required to provide the coded output. If printed Braille could be made popular, such a machine would provide a very economical link between the blind and the printers' art.

Acknowledgment is made to the National Research Council of Canada (Ottawa) for financial support of part of the work.

[1] D'Albe, E. E. Fournier, *Nature*, **105**, 295 (1920).

[2] D'Albe, E. E. Fournier, *Electrician*, 183 (Aug. 13, 1920).

[3] *Vancouver Sun* (Vancouver, B.C.), "Electronic Eye Reads for the Blind", Dec. 8, 1960. This is a Press report of the work in England and is typical of many put out recently.

[4] Abma, J. S., Huffman, L. L., Mason, L. J., and Coffey, J. L., "The Further Development and Evaluation of Aural Reading Devices for the Blind", *Rep. Battelle Memorial Inst.* (June 30, 1960).

[5] Zahl, P. A., edit., *Blindness, Modern Approaches to the Unseen Environment* (Princeton Univ. Press, 1950).

[6] Summary, Second Tech. Session on Reading Machines for the Blind (Sept. 7, 1958). Filed with: Chief of Research and Development Division, Prosthetic and Sensory Aids Service, Veterans Administration, 252 Seventh Avenue, New York 1.

[7] Kocher, D. G., M.Sc. thesis, Mass. Inst. Tech. (June 1959).

[8] Cooper, F. S., Delattre, P. C., Liberman, A. M., Borst, J. M., and Gerstman, L. J., *J. Acoust. Soc. Amer.*, **24**, 597 (1952).

[9] Shepard, D. H., "Apparatus for Reading", Patent *M* 2,663,758 (Assigned to IBM machines, Dec. 22, 1953).

[10] Taylor, W. K., *Proc. Inst. Elec. Eng.*, B, **106**, 198 (1959).

[11] Horwitz, L. P., and Shelton, G. L., *Proc. Inst. Radio Eng.*, **49**, 175 (1961).

THERMAL SHOCK AND ITS EFFECT ON THERMISTOR DRIFT

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IN 1948, one of us (J. H. S.) undertook an investigation of sub-surface temperatures in drill-holes in Navy Petroleum Reserve No. 4 as a part of a study of permafrost problems in arctic Alaska. Early measurements were made with copper-coil resistance thermometers. Beginning in 1949, however, thermistors were used as the temperature-sensing element because of their high thermal sensitivity. These were mounted in a multiconductor cable employing a circuit designed to permit the use of a minimum number of conductors for a given number of thermistors and to allow a correction for temperature distribution along the wires[1]. In construction the cable jacket was slit to permit the insertion of the thermistors in the appropriate conductors. Originally the slits were closed by wrappings of pressure-sealing vinylite tape. Later the cable slits were sealed by special vulcanizing techniques.

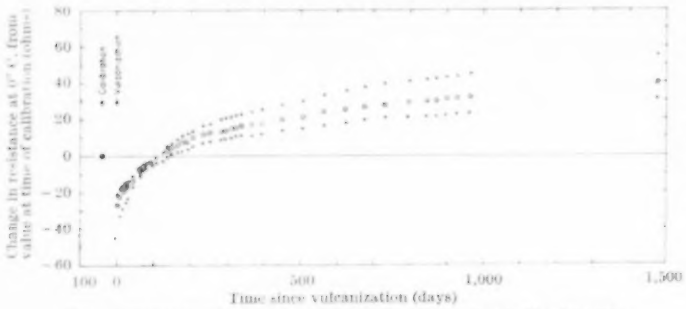

Fig. 1. Change in resistance at 0° C. with time after vulcanization (at 120°–130° C.) for 56 thermistors vulcanized in cables 199 and 200. ○, Mean of all 56 thermistors, cables 199 and 200; ×, thermistor 3786 (minimum change); +, thermistor 3834 (maximum change)

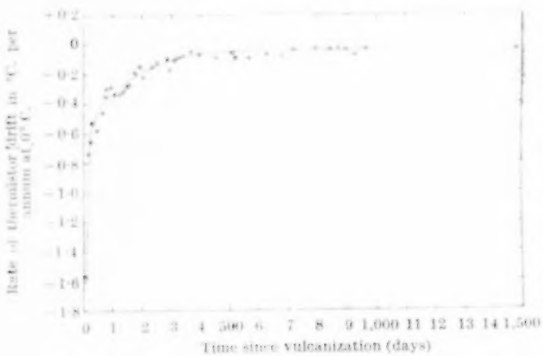

Fig. 2. Change in the rate of temperature drift with time for the mean of the 56 thermistors in cables 199 and 200

It was soon found that thermistor calibrations were disturbed by the vulcanization process. It was thought that this might be due to either of two factors: (1) chemical effects caused by free sulphur during vulcanization; (2) thermal shock caused by the heat of vulcanization. Experiments with litharge rubber, furnished through the kindness of the Rubber Section of the National Bureau of Standards, to eliminate most of the free sulphur during vulcanization, showed no apparent reduction of the effect. Nor was the effect either eliminated or reduced when a plastic-insulated cable was employed. This supported the idea that the effect was due largely, if not entirely, to thermal shock.

To test this hypothesis 12 thermistors were placed in a clean mould and raised to vulcanizing temperatures (120–130° C.) for 1 hr. All twelve showed the same typical calibration disturbance as those vulcanized in a cable.

Since that time some 80 thermistors have been investigated for the effects of thermal shock, and their subsequent calibration drift has been studied by recalibrations at approximately regular intervals in either a high-precision temperature-controlled bath or in an ice-bath. In particular, the resistances of 56 thermistors in two vulcanized cables have been rechecked in carefully prepared ice-baths, first at weekly, later at two-, three- and four-weekly intervals over a period of 961 days (2·6 years) with a later follow-up check at 1,475 days (4·04 years). This work has indicated certain generalizations to hold for the thermistors investigated (mostly type 17A, material No. 1 composition, disk-shaped). These were mostly a commercially available type composed of manganese and nickel oxides, disk-shaped, approximately 0·2 in. in diameter and 0·04 in. thick, with axial leads attached by silver-eutectic solder to a ceramic silver button attached to the face of the disk; at room temperatures its resistance is approximately 1,000 ohms and its rate of change of resistance with temperature approximately 4·4 per cent per deg. C.

(1) Of 70 thermistors heated to vulcanization temperatures the calibrations of all but one were offset in the heating direction, that is, after vulcanization their resistance at a given temperature was found to be lower than before vulcanization so that they registered too high an apparent temperature. For 55 of the 56 thermistors in the two vulcanized cables, for example, there was a decrease in resistance after vulcanization of 18–45 ohms, resulting in an increase in the apparent temperature of the ice-bath of 0·11–0·28° C. with an average of 0·20° C. as measured by the two cables. The one aberrant thermistor, No. 3,800, showed an increase in resistance after vulcanization of 1·9 ohms corresponding to a decrease of − 0·01° C. in the apparent temperature of the ice-bath.

Following the initial offset, all the heated thermistors began to increase in resistance (Fig. 1), returning exponentially towards their pre-vulcanization resistance. However, instead of approaching this value asymptotically, as had been expected, they reached this value after approximately 120 days, crossed over it, and continued to increase in resistance, but at a gradually diminishing rate. After four years they are still continuing to change, but at a slow and apparently nearly uniform mean rate of approximately 6 ohms per annum, equivalent to a decrease in the apparent temperature of the ice-bath of approximately 0·036° C. per annum (Fig. 2). The aberrant thermistor, No. 3,800, after the initial abnormal offset has shown a normally increasing resistance (decreasing apparent temperature) and has in fact closely paralleled the drift of the normal thermistors, as seen in Fig. 3.

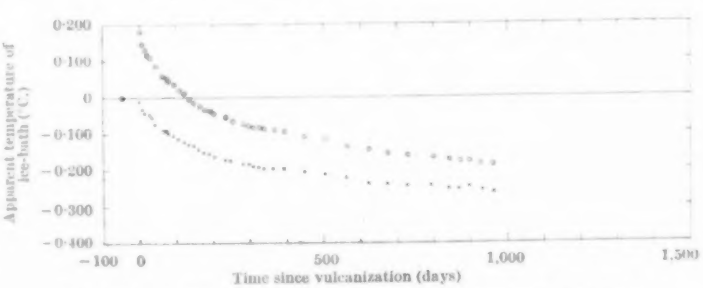

Fig. 3. Change of the apparent temperature of the ice-bath with time after vulcanization (at 120°—130° C.) as measured by the mean of 56 thermistors in cables 199 and 200 (○), and by thermistor No. 3800 (×)

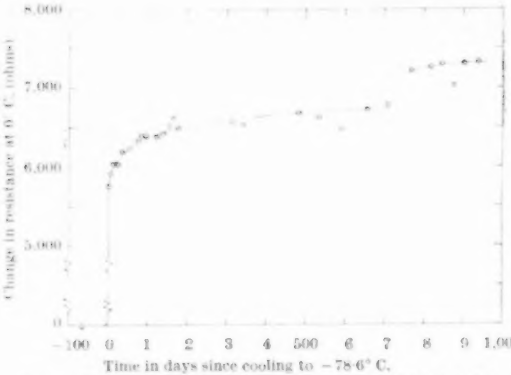

Fig. 4. Change with time in the mean resistance at 0° C. of 12 thermistors which were cooled to −78·6° C. at $t = 0$ days. The offset at 766 days was caused by a measurement at −30° C. made at $t = 715$ days following a long period at temperatures not lower than 0° C. Note that the vertical scale in this figure is 25 times that of Fig. 1

(2) Because heat shock offset the calibration in the 'hot' direction it was thought that cold-shock might produce an offset in the 'cold' direction, that is in the direction of increased resistance. Accordingly 12 thermistors were wrapped in paper and placed next to a block of dry ice (− 78·6° C.) for 15 min., then unwrapped and placed in contact with the dry ice for 1 hr. They were then allowed to return slowly to the temperature of the room and recalibrated. As was anticipated, all were found to have been offset to a higher resistance when rechecked in the ice-bath. The effect was, however, much more severe than in the case of the heated thermistors, the mean resistance of the 12 cooled thermistors at 0° C. having increased 5,754 ohms (Fig. 4). Of the 12 thermistors tested two were not greatly affected. The remaining 10, however, were seriously disturbed, one thermistor, No. 3,538, having its resistance increased nearly 500 per cent. The corresponding offsets in the apparent temperature of the ice-bath ranged from − 0·10° to − 29·73° C., with a mean offset for all 12 thermistors of − 18·91° C. This may be compared with a mean offset of only + 0·20° C. both for the 12 heated thermistors and for the 56 thermistors vulcanized in cables 199 and 200.

Following this initial 'cold-shock' offset the resistances of the 'frozen' thermistors did not, however, return towards their pre-shock values. Instead they too continued to increase exponentially at a gradually diminishing rate which, however, exceeded that of either the normal or the heat-shocked thermistors, as seen in Fig. 4. It may also be noted that the 'frozen' thermistors tended to become somewhat erratic, so that it was difficult at times to obtain a satisfactory bridge balance.

Because of the greatly increased resistance, as well as the erratic character, of some of the readings it was thought possible that the rather rapid chilling might have caused actual physical damage to the 'frozen' thermistors. A careful examination of all 12 thermistors was made under a microscope at magnifications up to × 100. Three of the twelve showed very fine, hair-line cracks in the side of the disk extending for short distances more or less parallel to the faces of the disk. These three were the most seriously disturbed of the 12, and thermistor No. 3,858, the most seriously disturbed of the three, was also the one with the most pronounced crack. The remaining 9 thermistors showed no evidence of any physical damage. This does not, of course, preclude the possibility of internal strains or lattice dislocations not externally visible.

(3) The thermistor drift after the initial thermal-shock offset, in all 80 thermistors investigated, was always an increase in resistance with time, although at a gradually diminishing rate of change, whether the thermal shock was due to heat or cold,and whether the initial shock-offset was plus or minus.

(4) Evidence from arctic measurements had indicated that thermistors permanently installed at points of constant temperature had a much smaller calibration drift than those exposed to variable temperatures. Accordingly a thermistor, No. 3,538, which had been subjected to more thermal shocks than usual, was placed in an ice-bath and kept continuously at 0° for 2·6 years. During the 269 days prior to this it had been vulcanized at 125° C., calibrated three times in a hypsometer at 100° C., and used for temperature measurements in a drill hole at 95° C. It would therefore have been expected to be more disturbed than the usual thermistor and subject to a faster rate of drift. Despite these facts, as seen (Fig. 5), its drift at a constant temperature of 0° C. was only 0·4 that of the normal vulcanized thermistor exposed to a variable temperature.

That this was not due to a naturally low drift-rate is shown by the two ice-bath determinations at − 47 and − 5 days in Fig. 5. The last previous heat shock was at − 242 days. Despite recovery periods, therefore, of 195 and 237 days respectively, those readings show a rate of change slightly greater than the mean after that recovery time for the 56 thermistors in cables 199 and 200.

(5) Because of the characteristic drift of the thermistors investigated it was found possible to use the drift curve to make corrections to an accuracy of the order of one or two hundredths of a degree Celsius over a 2·6-year period within which the calibration changed as much as 0·6° C.

In the light of these facts, it is evident that thermistors should be protected from large and sudden changes in temperature, whether hot or cold. Serious cold-shock is especially to be avoided. Room-temperature vulcanization is possible with special rubber compounds and accelerators, as well as with certain plastics. Pressure-sealing tapes may be used where they give adequate protection against leakage or the entry of water into the cable.

Calibrations should be made at the approximate temperature to be measured and should be restricted

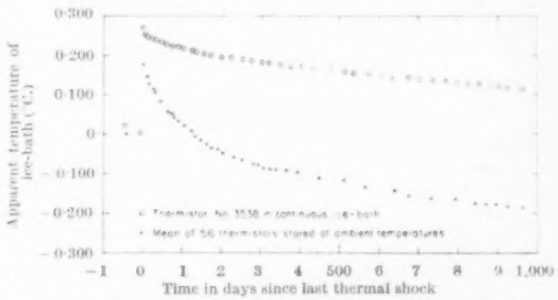
0·300
0·200
0·100
0
− 0·100
− 0·200
− 0·300
Apparent temperature of ice-bath (° C.)
Thermistor No. 3538 in continuous ice-bath
Mean of 56 thermistors stored at ambient temperatures
−1 0 1 2 3 4 500 6 7 8 9 1,000
Time in days since last thermal shock

Fig. 5. Changes in the apparent temperature of the ice-bath with time (after hypsometer test at 100° C.) as measured by thermistor No. 3538 kept continuously at 0° C., compared with those measured by 56 thermistors vulcanized in cables 199 and 200 and stored at ambient temperatures between ice-point measurements

to as narrow a range on either side of that value as is feasible.

Thermistors which have been subjected to thermal shock should be allowed a sufficient subsequent rest period to allow their return to a normal drift-rate. They should be recalibrated just prior to, or just after, subsequent measurements, or both, depending on the precision desired and the length of the measurement period involved. If possible the thermistors used should be kept continuously at the temperature being measured for the entire measurement period, especially during a long-continued measurement series, in order to reduce thermistor drift to a minimum. With these precautions drift can be reduced to very small values. These values may often be still further reduced by properly applied corrections.

Publication of this investigation is authorized by the Director of the U.S. Geological Survey.

[1] Swartz, J. H., *Science*, **120**, 573 (1954); *U.S. Geol. Survey Prof. Paper 269-U*, 711 (1958).

TWILIGHT AND THE 'CREP' UNIT

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FOR a very long time many kinds of animals have been known to be most active around sunset. A relationship between the changing light intensity and activity is now usually presumed, and it has been shown[1] that the duration of the swarming of mosquitoes depends on the duration of twilight.

Civil twilight is the period from sunset to the time when darkness compels man to suspend labour in the open air. Similarly, the beginning of dawn in the morning is the moment when the light becomes sufficient for the resumption of normal human activity. In this article the discussion will be confined to conditions at sunset with the tacit understanding that corresponding conditions prevail at sunrise.

Even if the end of civil twilight is rather loosely defined it has long been known[2] that several natural phenomena occur at the very end of man's day: (1) stars and planets of the first magnitude are just becoming visible; (2) the purple light above the sunset disappears; (3) the antirepusecular arch passes zenith (this is the borderline between the reddish tinged and the ashy or deep blue part of the sky[3]; (4) the centre of the Sun is about 6° below the horizon. The last point permits an unequivocal definition of the end of twilight: it is the moment when the Sun's altitude is − 6° 00′.

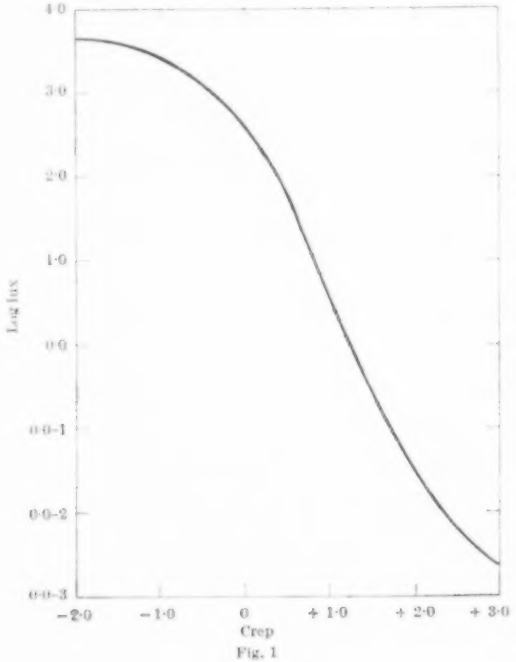

Fig. 1

The definition of the beginning of twilight depends on the various definitions of sunset. In most of the tables now in use[3-5] sunset is defined as the moment when the uppermost part of the Sun appears to coincide with the horizon. Due to the refraction of the atmosphere the Sun will at that moment be about 34′ below the horizon, and as the half diameter of the disk of the Sun is about 16′, the Sun's altitude at the moment of sunset is actually about − 50′. The refraction changes with the atmospheric conditions, and the sunset may be observed to occur one or even a couple of minutes in variance with the moment to be expected from astronomical tables. The duration of civil twilight given in such tables is the number of minutes required for the position of the Sun to change from − 50′ to − 6° 00′. The duration varies according to geographical latitude and season from 21 min. to several hours.

The effect of twilight on the habits of animals is caused by the change in illumination. The unit of illumination is the lux. It is convenient, and, according to Weber–Fechner's law, also the most correct, to operate with the logarithms of lux. The illumination is best measured as the diffuse light from the sky incidental to a horizontal plane. If the sky is clear the illumination depends almost exclusively on the altitude of the Sun. At sunset it is thus 2·60 log lux (400 lux), and at the end of twilight it is 0·55 log lux (3·5 lux). Biological phenomena depending on the illumination should therefore be related to the Sun's altitude rather than to the hour angle. Instead of using hours and minutes to describe the time-sequence of such habits of animals it is more convenient and logical to use a time unit based on the duration of twilight, especially when observations made at different latitudes and in different seasons have to be compared. In work now in progress on the comparative ethology of swarming of mosquitoes it has been found very useful to transform all time indications into such twilight values, called 'crep' (from *crepusculum*). One crep is defined as the number of minutes which, under the given conditions, correspond to the duration of twilight. Hours and minutes are changed to crep values by means of the expression:

$$\frac{\text{time of day} - \text{time of sunset}}{\text{duration of twilight}}$$

and correspondingly:

$$\frac{\text{time of sunrise} - \text{time of day}}{\text{duration of twilight}}$$

If sunset is at 18 h. 00′, and the twilight lasts 30 min., the hour 19 h. 00′ will be + 2·00 crep, and 17 h. 15′ will be − 1·50 crep. The values of crep are positive when they refer to the period during which the Sun is below the horizon, negative for periods after sunrise to before sunset. Sunrise and sunset have the crep value 0, while the end of twilight in the evening and the beginning of dawn have the values + 1·00 crep.

When the sky is clear a certain illumination corresponds to any given value of crep. Using the data of Kimball[2], Provost[6] and my own measurements from Florida, Iraq and Denmark, a table of corresponding values has been prepared; it will be published later[7], and is represented here as Fig. 1.

White clouds reflecting sunlight may give higher illuminations than those of the table, and lower values may be found when the sky is covered by dark clouds. Especially after sunset the differences are usually small compared with the rapid change of illumination. During a recent field investigation in Denmark the sunset illumination (2·60 log lux) occurred at the calculated minute on 21 out of 49 evenings; on 22 evenings this illumination occurred at an average of 0·1 crep (3½ min.) before sunset. On 6 evenings it became dark so quickly that the illumination was reduced to 2·60 log lux at 0·20–0·84 crep before sunset.

Fig. 1 shows that at least the middle part of the curve approximates a symmetrical S-shape with the turning point at + 1·00 crep. We have thus one more characteristic of the end of twilight: it is the moment when the illumination changes from an accelerating rate of change to a decelerating rate.

At places where animals are resting the illumination is often lower than in the open; however, there is usually a simple relationship between the illumination at such places and that measured in the open.

The calibration of light-meters often meets with difficulty because the lux is not defined purely as a physical unit. It is based on the curve of photonic relative luminous efficiency[9], which is an expression for the relative sensitivity of the human eye to light of different wave-lengths. A light-meter calibrated by means of a standard light source can only be used in the field by means of special filters. It is easier to calibrate the instrument by measuring the illumination in arbitrary units on a few clear evenings, and by means of the crep/(log lux) function to find the relationship between the arbitrary units and the illumination.

[1] Nielsen, E. T., and Nielsen, A. T., *Ecology*, **34**, 141 (1953).
[2] Kimball, H. H., *Monthly Weather Rev., November 1916*, 614 (1916).
[3] *Smithsonian Meteorological Tables*, sixth edit., *Smithsonian Misc. Coll.*, **114** (1951).
[4] *The American Ephemeris and Nautical Almanac* (U.S. Naval Observatory, Washington).
[5] *The Air Almanac* (U.S. Naval Observatory, Washington, and H.M.S.O., London).
[6] Provost, Maurice W. (personal communication).
[7] Nielsen, E. T., and Nielsen, H. T., *Swarming of Danish Mosquitoes* (Entom. Medd. Copenhagen, in the press).
[8] *Vocabulaire International de l'éclairage* (Commission Internationale de l'éclairage, Bureau Central, Paris).

FOOD SELECTION BY SILKWORM LARVÆ, *BOMBYX MORI*

Citral, Linalyl Acetate, Linalol, and Terpinyl Acetate as Attractants of Larvæ

ONE of us (Y. H.)[1] has reported on the mechanism of food selection of silkworm larvæ, and has pointed out with regard to a principle of food selection that silkworms are attracted by three stimulants in mulberry leaves, namely, attractant, biting factor and swallowing factor. The attractant only induces the larvæ to the food and the biting factor raises the action of biting and the third, swallowing factor, helps the larvæ to swallow the food continuously. Agar jelly containing these three stimulants is eaten by the larvæ as from the mulberry itself.

This communication is concerned with the attractiveness of some terpenes for silkworms and the existence of citral, linalyl acetate, linalol, and terpinyl acetate in mulberry leaves.

As already described[1], the ether-soluble fraction of methanol-soluble matter from fresh mulberry leaves attracts silkworms. When a small amount of active carbon is added to this ether fraction the yellowish ether solution is obtained as a result of the absorption of green substances. This yellowish solution powerfully attracts the larvæ (Table 1). The neutral fraction of the ether solution, which is fractionated by washing with a 1 per cent solution of sulphuric acid and a 2 per cent solution of sodium carbonate in this order, and the steam distillate of this neutral fraction are also powerful attractants (Tables 2 and 3). The yield of an active fraction in this distillate is about 0·2 gm. per 4 kgm. fresh leaves. The ultra-violet absorption curve of this distillate resembles that of terpene alcohols, and the infra-red absorption spectra also closely resembles that of terpinyl acetate, and further detection by gas chromatography suggests the existence of citral, linalyl acetate, linalol and terpinyl acetate in this fraction. The attractive force was tested on the pure chemicals, citral, terpinyl acetate and some terpene alcohols (Table 3).

Six small circles along the circumference of a round filter paper are drawn in equal intervals and the paper is set in a shale (diameter: 8·5 cm.). Samples absorbed on cellulose powders are prepared as follows. A certain amount of the solution of the samples is absorbed on 0·25 gm. cellulose powder, and solvent is evaporated in the air, and then water is sprayed on it: on the other hand, the same amount of cellulose powders containing a small amount of water is prepared as control. These cellulose powders are divided into three portions respectively and put on six circles reciprocally. When the test on the difference of activities between *A* and *B* is taken in a set, the powders are put on in the order *A*, *B*, control, *A*, *B*, and control. Thirty hatched larvæ are placed on the centre of the filter paper. After leaving the set at 24° C. for a certain time, the number of larvæ gathered on each powder and wandering on the intermediate

Table 1. Number of Hatched Silkworms gathered on the Cellulose Powder

Amounts of sample sprayed on cellulose powder correspond to that in 2 gm. of powdered mulberry leaves

	30 min.	75 min.	120 min.
Ether solution	15	23	23
Hexenol	8	6	6
Control	0	0	1
Intermediate space	7	1	0
Total	30	30	30

Table 2

	30 min.	75 min.	120 min.
Neutral fraction	17	21	22
Acidic fraction	2	3	3
Basic fraction	0	0	0
Intermediate space	11	6	5
Total	30	30	30

Table 3

	10 min.	30 min.	60 min.
Steam distillate	13	23	25
Non-distillable fraction	7	3	1
Control	5	1	0
Intermediate space	5	3	4
Total	30	30	30

Table 4

Conc. of substrate	1/5			1/2			1			3			5		
Position (substrate)	*S*	*C*	*I*	*S*	*C*	*I*	*S*	*C*	*I*	*S*	*C*	*I*	*S*	*C*	*I*
Terpinyl acetate*	10	6	14	9	3	18	13	6	11	10	8	12	*16*	10	4
Linalyl acetate*	19	7	4	*25*	1	4	17	12	1	17	11	2	19	3	8
Linalol*	14	4	12	11	2	17	20	0	10	22	2	6	21	8	1
Citral*	*20*	7	3	19	6	5	13	13	4	6	13	11	10	15	5
Terpineol							2	15	13						
Geraniol							0	12	18						
Geranyl acetate							3	15	12						
Oxycitronellal							0	17	13						
Hexenol*	11	2	17	12	3	15	13	4	13	11	2	17	6	8	16

Concentration 1 means that 1 c.c. of 10 mgm. per cent ethereal solution of substances was absorbed by 0·25 gm. cellulose powder and the powder was divided into three portions as described above, 1/2 means 1/2 c.c. of the solution and so on. *S*, *C* and *I* mean sample, control and intermediate space, respectively. Numbers of the larvæ are counted after 1 hr. at 24° C. Substances marked with an asterisk are those presumed to exist in mulberry leaves by gas-chromatographic techniques; others do not exist in the leaves.

space are counted. The results of the test are given in Tables 1–4.

Thus, from these experiments, citral, linalyl acetate, and linalol, which are seen to exist in mulberry leaves, are very attractive to silkworm larvæ, and terpinyl acetate and hexenol[2] are less attractive. Other terpenes shown in Table 4 which have not been detected in mulberry leaves do not attract. These terpenes attract silkworm larvæ but do not stimulate biting.

We wish to thank Dr. Teruhiko Hosoi for his advice and Dr. H. Okamura of the Eikodo Co., and Dr. M. Ono of the Institute of Chemistry, Kyoto University, for the chemically pure perfumes and β-γ-hexenol, respectively.

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Ken-ichi Naito

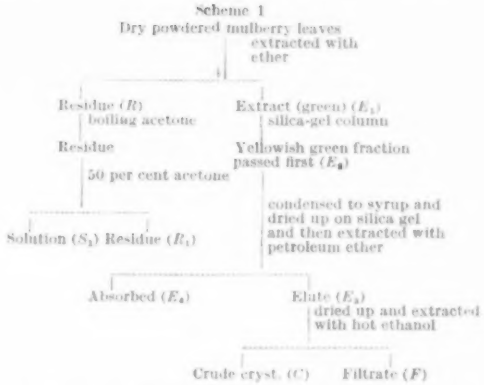
[1] Hamamura, Y., *Nature*, **183**, 1746 (1959).
[2] Watanabe, T., *Nature*, **182**, 325 (1958).

β-Sitosterol as one of the Biting Factors

Dry powdered mulberry leaves were extracted with ether and the extract was fractionated as in Scheme 1.

E_1 markedly attracts and stimulates the biting action of silkworm larvæ as described[1]; E_2 and E_3 are also positive in both respects. Crude crystal (*C*) from E_3 strongly stimulates biting but is not an attractant. On the contrary, filtrate (*F*) scarcely stimulates biting but is a strong attractant (Table 1). Therefore, it is possible to distinguish the biting factor from the attractant in the mechanism of food selection by silkworms.

Scheme 1



The crude crystal (*C*) from E_3 shows a strong Liebermann's sterol reaction. Thus the active principle to stimulate the biting action seems to be a sterol-like substance. Two of us (Y. H. and K. N.)[2] isolated β-sitosterol in a chemically pure state from mulberry leaves. As Table 2 shows, β-sitosterol showed strong activity on the biting test on agar thread which was softened with a small amount of water and sprayed with an ethereal solution of β-sitosterol. Other sterols, cholesterol and ergosterol, gave little activities on this test (Table 2).

Hobson reported[3] that a fat-soluble accessory growth factor required by all insects is cholesterol; Fraenkel and Blewett have stated that sitosterol is utilized in place of cholesterol by phytophagous insects. But we have found that β-sitosterol is required as a biting factor in the mechanism of their food selection, since β-sitosterol, not only on agar thread but also on glass, stimulates biting, and although cholesterol and ergosterol probably have higher nutrition value than β-sitosterol, they give lower activities on the tests of both biting and swallowing actions as shown in Tables 2 and 3.

In Table 3, a set of test dishes requires a much larger amount of β-sitosterol (20 mgm.) in comparison with the sterol content in mulberry leaves (about 0·2 per

Table 1

	Test of attraction: No. of larvæ gathered on, Total larvæ, 30				Test of biting action				
	I	II	III	IV					
E_2	28				+	+	+	+	+
E_3		28			+	+	+	+	+
C			4		+	+	+	+	+
F				28	+	−	−	−	−
Control	0	0	12	0	−	−	−	−	−
Intermediate	2	2	14	2					
Total	30	30	30	30					

Test of attraction was done by the method described in the preceding communication. In the test of biting action, + + + + + denotes that all larvæ bite the agar thread and − − − − − denotes none of larvæ does.

Table 2

	Test of biting action
β-Sitosterol (conc.)	+ + + + +
β-Sitosterol (dil.)	+ + + + −
Cholesterol (conc.)	+ + + − −
Ergosterol (conc.)	+ + − − −
Control	− − − − −

Table 3

	Test of swallowing (number of faeces)
Basal diet (B.d.) only	26
B.d. + leaf powder (0·3 gm.)	262
B.d. + β-sitosterol (20 mgm.)	223
B.d. + β-sitosterol (4 mgm.)	116
B.d. + β-sitosterol (20 mgm.) (R_1 absent)	47
B.d. + cholesterol (20 mgm.)	16
B.d. + ergosterol (20 mgm.)	44

cent). Doubts may be expressed concerning the relation between the concentration and the activity unless it is supposed that there is an accumulation of β-sitosterol on the surface of mulberry leaves. It has been proved that when the leaves are wiped with an absorbent cotton containing a small amount of ether, the cotton strongly stimulates biting, and as a matter of course indicates a positive reaction for Liebermann's sterol test.

The swallowing test by newly hatched larvæ was made using pure β-sitosterol in place of the crude one (E_1 or E_2) by the modified method already described[1]. One basal diet consists of the following: 3 c.c. 2 per cent agar solution containing 1 per cent sucrose, 0·2 gm. cellulose powder and 0·3 gm. of R_1 which seems to have a swallowing factor (diameter of a Petri dish: 4·5 cm.). Ten newly hatched larvæ were put on an agar diet for 18 hr. at 24° C. and the feces were counted (Table 3).

From Table 2 it is concluded that β-sitosterol is the biting factor and some sterols may be an accessory in mulberry leaves. From Table 3 it is clear that the larvæ require an unknown swallowing factor together with the biting factor, β-sitosterol, for their complete food taking, and the amount of food eaten is controlled by the concentration of β-sitosterol.

Further experiments suggested the existence of another water-soluble biting factor in the S_1 fraction.

We wish to express our thanks to Dr. T. Hosoi for his advice. This work was supported by a grant from the Ministry of Education.

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[1] Hamamura, Y., *Nature*, **183**, 1746 (1959).
[2] Hamamura, Y., and Naito, K., *J. Agric. Sci. Japan* (in the press).
[3] Roeder, K. D., *Insect Physiology*, 367 (John Wiley and Sons, Inc., New York, and Chapman and Hall, Ltd., London, 1953).

CYCLICAL FEEDING-ACTIVITY IN COLONIZED MOSQUITOES

By Dr. J. D. GILLETT
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EXTENSIVE field-studies on African mosquitoes made over the past 18 years by Haddow and others[1] have demonstrated the cyclical nature of biting activity. These investigations show that a species usually exhibits a characteristic biting pattern, although this is not always constant throughout its range; they do not, however, show to what extent such patterns are a direct response to environmental stimuli, or to what extent they represent an expression of inborn rhythms. Such work has been based on the catching, and removal from the population, of female mosquitoes that alight on the bait, the mosquitoes so removed in unit time being sorted and counted at leisure. Clearly such a method depends on the presence of what, for practical purposes, can be regarded as an infinite population of mosquitoes, and this automatically precludes its use if biting activity is to be studied under controlled laboratory conditions. Yet it is precisely this approach that is now urgently needed[2]. The problem can, however, be studied in the laboratory if, instead of counting the number of mosquitoes that alight on the bait, we measure the amount of food they remove from it. The present article describes an experiment to test this method, using sugar solution as a source of food.

An apparatus has been devised which provides a continuous supply of food from a graduated tube. The apparatus was developed independently from, and it differs in principle from, the feeding apparatus described by Rodhain *et al.*[3], which allowed tsetse flies, *Glossina*, to suck blood through a mouse- or rat-skin membrane. They used an open graduated pipette in order to record the hydrostatic pressure of the blood, but mentioned that this would also allow measurement of the amount of blood ingested by each fly. The principle of the present apparatus is to record the amount of fluid removed from the bait in a given period of time as a measure of feeding activity. To do this it was essential that the apparatus be capable of feeding a large number of insects over a continuous period of several days. Changes in attractiveness were reduced by the use of perforated polyethylene or of fine-mesh metal gauze in place of animal skin. The alternative choice of metal gauze as a feeding surface was partly influenced by the description of an ingenious feeding device given by Dr. P. A. Woke at the eleventh International Congress of Entomology held in Vienna during August 1960.

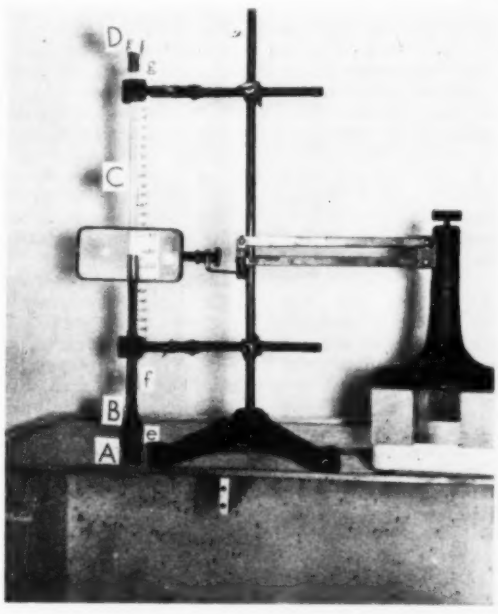

Fig. 1. Apparatus for recording the amount of fluid removed from the bait as a measure of cyclical activity in fluid-feeding insects

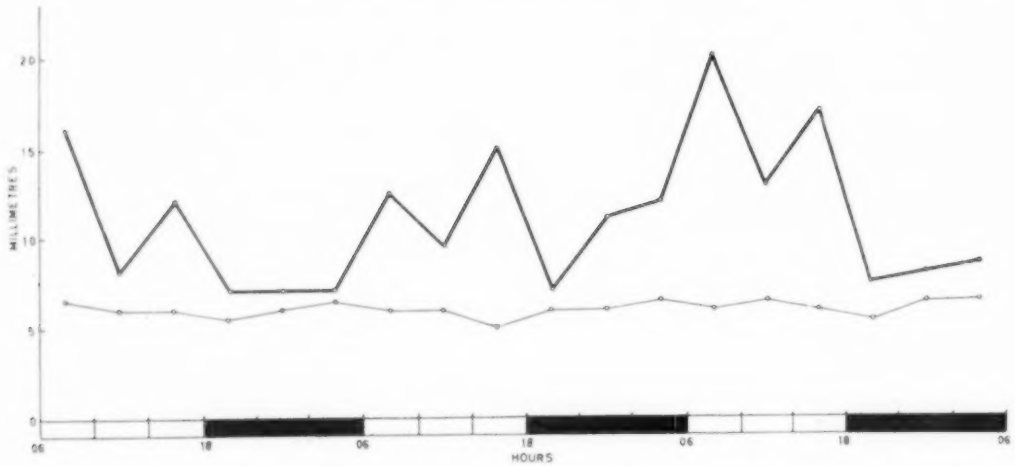

Fig. 2. Sugar feeding-cycle in the mosquito *A. aegypti*. Thick line: loss of fluid each 4 hr. through feeding plus evaporation (test series); thin line: loss of fluid each 4 hr. through evaporation only (control series). Light switched on 06–18 hr. (East African Standard Time) each day

The apparatus (Fig. 1) as used here consists of a wide feeding-tube, *A*, closed at the lower end by a 0·5-mm. mesh, non-corrosive, non-absorbent perforated cap, and connected above by a tapering middle-piece, *B*, to a narrow, transparent measuring-tube, *C*, graduated in mm. (7·0-mm. internal diameter and 300 mm. in length). These three parts are joined together by two pieces of flexible tubing (*e* and *f*), the latter being long enough (about 60 mm.) to allow flexure through 90° without occlusion. The open upper end of the measuring tube is attached to a short piece of flexible tubing, *g*, which can be closed by means of a screw-clip, *D*.

To prepare the apparatus for use, screw-clip *D* is left open, and the whole apparatus is bent at *f* to form a U-tube. Feeding-fluid is introduced, until the whole apparatus is nearly full. The two limbs of the U-tube are then adjusted until the fluid reaches the perforated end of the feeding-tube in one limb, and nearly to the top of the measuring-tube in the other. Screw-clip *D* is then closed and the apparatus is straightened out to a vertical position, with the feeding-tube at the lower end. It is placed on the gauze top of a cage containing the mosquitoes, the perforated end of the feeding-tube being in direct contact with the gauze top of the cage.

Fluid will be lost from the apparatus by two means: evaporation and mosquito-feeding. Allowance for the amount of fluid lost through evaporation can be made by using a duplicate apparatus over an empty cage as a control; the difference in loss of feeding-fluid in the two tubes can then be taken as a measure of feeding activity in a given time. With the dimensions given above, a drop of 0·5 mm. on the scale records a volume of $19{\cdot}24 \times 10^{-6}$ litre (19·24 µl.). For practical purposes this can be taken as roughly equivalent to five female-mosquito meals[4]. The estimate would, of course, vary according to species and strain used and will probably be different if both sexes were feeding on the fluid.

Two series of observations were run concurrently: a control series using the apparatus with 10 per cent w/v sugar solution (5 per cent glucose, 5 per cent sucrose) over an empty cage, and a test series using a similar arrangement over a cage of mosquitoes. These were *Aedes* (*Stegomyia*) *aegypti* (L.) from Ilobi, Nigeria, and had been colonized in Entebbe for two years. Until the day before the experiment was started, the mosquitoes had had access to raisins (continuously) and to blood (infant mice for 1 hr. a day). Throughout the experiment an egg-laying funnel was present[5]. The experiment was carried out under controlled conditions of temperature (28° C.) and humidity (70 per cent relative humidity) with an artificial light regimen of 12 hr. light each 24 hr. Observations were made every 4 hr. for 3 consecutive days and nights.

Table 1. Feeding-cycle in the Mosquito *A. aegypti* under Conditions of 12 hr. Light each 24 hr., expressed as the Amount of Fluid removed from the Bait each 4 hr.

Date	Time (E.A.S.T.)	Fluid loss in mm.		
		(*a*) Test	(*b*) Control	(*a*-*b*) Difference
30.10.60	0600	16·0	6·5	9·5
	1000	8·0	6·0	2·0
	1400	12·0	6·0	6·0
	1800	7·0	5·5	1·5
	2200	7·0	6·0	1·0
31.10.60	0200	7·0	6·5	0·5
	0600	12·5	6·0	6·5
	1000	9·5	6·0	3·5
	1400	15·0	5·0	10·0
	1800	7·0	6·0	1·0
	2200	11·0	6·0	5·0
1.11.60	0200	12·0	6·5	5·5
	0600	20·0	6·0	14·0
	1000	13·0	6·5	6·5
	1400	17·0	6·0	11·0
	1800	7·5	5·5	2·0
	2200	8·0	6·5	1·5
2.11.60	0200	8·5	6·5	2·0
	0600			

The results are shown in Table 1 and in Fig. 2. The difference between the two series is very marked: whereas in the control the rate of loss of fluid is almost steady at 6 mm. each 4 hr., in the test series the rate fluctuates, showing two peaks in each light-'stretch', one in the first 4 hr. light-'period', another in the last (the terms 'stretch' and 'period' have been defined previously for use in this sort of work[6], and are used in the same sense here).

During the final 12 hr. light-stretch, observations were made hourly, in order to obtain a preliminary analysis of the two peaks. The results for this single 12-hr. stretch indicate that the two peaks are different in form—that in the first 4-hr. light-period being confined to the single hour following onset of light, that in the last 4-hr. light period being less concentrated.

It is not claimed that the feeding-cycle obtained in the present experiment represents the definitive cycle for the species, or even for the strain used. This particular cage of mosquitoes had previously been supplied with a blood-meal at a set time each day, and an acquired blood-feeding rhythm may have influenced the sugar-feeding rhythm. Moreover, it is not known whether both sexes contributed equally to the two diurnal peaks of feeding activity. The results do, however, indicate that, with this apparatus as a tool, or with other similar apparatus employing the same principle, the way is now open for a detailed study of feeding-cycles along the lines already used in the study of mosquito oviposition-cycles[2,5,6]. It is planned to use the apparatus first with sugar solution or fruit juice, using male and female mosquitoes both separately and together, and later with vertebrate blood. Initially, observations will be made on an hourly basis, but when the cycles have been 'established', a study of the mechanisms involved may then be made on a 4-hr. basis. Improvements and modifications can doubtless be made on the prototype described here; the apparatus is, for example, particularly suitable for use with photographic recording.

Certain inherent difficulties have to be overcome before this method can be adapted for the study of blood-feeding cycles. While clotting can easily be prevented by one of the standard methods, sedimentation of the cells, or denaturing and precipitation of the blood proteins, presents a more difficult problem. Sedimentation can be retarded considerably by agitation, and in preliminary trials this has been achieved by convection set up by a heat exchanger coil wrapped around the feeding-tube. If laked blood is employed, it is necessary to use perforated polyethylene or to coat the metal gauze of the feeding-tube with a fine film of paraffin wax. The most promising results so far have come from the use of laked blood with a heat-exchanger coil. Details about dilutions and preservation will be given in a later communication.

[1] Haddow, A. J., Gillett, J. D., and Highton, R. B., *Bull. Ent. Res.*, **37**, 301 (1947). Mattingly, P. F., *ibid.*, **40**, 149 (1949). Haddow, A. J., *ibid.*, **45**, 199 (1954).
[2] Gillett, J. D., Corbet, P. S., and Haddow, A. J., *Ann. Trop. Med. Parasit.*, **53**, 132 (1959).
[3] Rodhain, J., Pons, C., Vandendranden, J., and Bequaert, J., *Arch. f. Schiffs. u. Trop. Hyg.*, **16**, 732 (1912).
[4] Boorman, J. P. T., *Ann. Trop. Med. Parasit.*, **54**, 8 (1960).
[5] Haddow, A. J., and Gillett, J. D., *Ann. Trop. Med. Parasit.*, **51**, 159 (1957).
[6] Gillett, J. D., Haddow, A. J., and Corbet, P. S., *Ann. Trop. Med. Parasit.*, **53**, 35 (1959).

LEAKAGE CURRENT RECTIFICATION IN THE SQUID GIANT AXON

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THE total current which flows across the membrane of the giant axon of the squid in response to stepwise changes in membrane potential in a voltage-clamp arrangement was shown[1] to consist mainly of sodium and potassium ions plus a small unidentified component, termed 'leakage'. This component was approximated by an equivalent conductance and apparent equilibrium potential, both constant with time and membrane potential.

We intended, in this work, to test these approximations and to determine, if possible, what ions might be involved in the leakage.

We used the standard, point-control voltage-clamp arrangement[2] and attempted to eliminate the currents due to sodium and potassium by means of the following procedure: (1) the membrane potential was controlled at a value close to the resting potential, during periods of measurement; (2) at intervals of about 1 sec. a 55 mV. hyperpolarizing pre-pulse of 7 msec. duration was followed immediately by the test pulse, either to a further hyperpolarized value or to the sodium equilibrium potential; (3) the membrane current at 0·4 msec. following the application of the test pulse was measured and taken to be the leakage current; (4) the sodium equilibrium potential was varied by substitution of choline ions for sodium ions in the external medium; (5) temperature was maintained at 10 ± 1° C.

For hyperpolarizing pulses sodium and potassium contributions to the leakage current are expected to be negligible, because the total current does not depend on the external sodium or potassium concentration (ref. 1 and this article). At the sodium equilibrium potential there is no net sodium current. If the depolarizing steps follow a hyperpolarizing pre-pulse, the onset of the potassium current is delayed[3] to such an extent that a negligible potassium current is expected during the first half millisecond.

We must distinguish between components of the total current, which are carried by sodium and potassium ions and are subject to the delayed rectification processes, and the possibility of an additional rectification with a very short delay. For depolarizations, a short time-constant increase in the potassium conductance might occur and not be observed as such.

In Fig. 1*A*, the leakage current is plotted as a function of membrane potential, for three typical

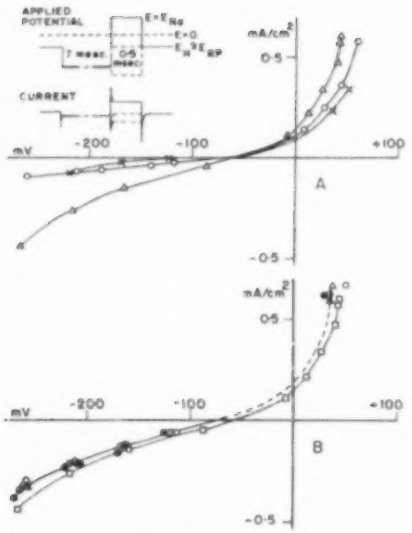

Fig. 1. *A*, leakage current versus membrane potential for three axons in varying concentrations of external sodium ion. Currents plotted were measured as indicated in the insert. E_H, holding potential just before the pre-pulse; E_{RP}, resting membrane potential; E_{Na}, sodium equilibrium potential. Zero current was taken as the current at 0·4 msec. after the application of test-pulse to the holding potential. Temperature, 10° C. ×, axon 60–47 with E_{RP} 67 mV.; ○, axon 60–61 with E_{RP} 66 mV.; △, axon 60–60 with E_{RP} 54 mV. *B*, leakage current versus membrane potential with 21 and 61 per cent of the normal external chloride. Curve for axon 60–60 replotted from Fig. 1 for reference. Temperature, 10° C. ○, artificial sea-water 1; ▲, 61 per cent chloride; ◑, artificial sea-water 2; △, 21 per cent chloride; ●, artificial sea-water 3; □, axon 60–60

axons. The insert in Fig. 1 indicates the method of measurement. The leakage current is not constant but exhibits marked rectification. The time-constant of delay was not obtainable with our system but is probably less than 100 μsec. In the hyperpolarized (more negative than the resting potential) region the curves showed no change on varying external sodium concentration from 430 to 43 m*M*/litre. The points associated with depolarizations to the sodium equilibrium potentials fall along a smooth curve. Axon 60–60 is typical of axons exhibiting low membrane resting and action potentials.

In an effort to identify the leakage-current charge-carriers we altered external chloride, potassium, calcium and magnesium. External chloride was altered by substitution with methyl sulphate.

Fig. 1*B* illustrates the results of measurements on axon 60–69 with one-half, and all, of the sodium chloride replaced by sodium methyl sulphate, giving a concentration of chloride of 61 and 21 per cent of the normal. The points in the depolarized region were obtained at the sodium equilibrium potential in normal sodium. For hyperpolarization there is clearly only negligible effect of chloride reduction. It is likely that this is true for the entire curve. The leakage curve for axon 60–60 is replotted from Fig. 1 for reference as being similar to axon 60–69. The steepness of the curve near the normal sodium equilibrium potential reduces sensitivity, but it would seem that here not more than 10 per cent of the leakage is accounted for by chloride ions.

In Fig. 2 the resting potential (*A*), and leakage current for a hyperpolarizing pulse to − 180 mV. following the standard pre-pulse (*B*), are plotted against time, while the external potassium, chloride and calcium and magnesium concentrations were varied. Since the resting potential, and probably the holding current, varied with time, there was some difficulty in comparing complete leakage curves. During periods of measurement, the membrane potential was held at a constant value regardless of the resting potential, introducing an uncertainty in the baseline to which leakage current is referred. However, the currents at a pulse potential of − 180 mV., measured in the usual way, are plotted as the circles in Fig. 2, giving the smooth curve through the four control values obtained in artificial sea-water. The current at 0·4 msec. following the pre-pulse relative to the current at the end of the pre-pulse is also plotted in Fig. 2*B* (triangles). For both cases the points obtained in 1/3 potassium and 1/5 chloride do not deviate from the line through the artificial sea-water points, while the points for 1/10 calcium and magnesium do. It is well known that lowering external calcium concentration tends to increase resting membrane conductance. It is important to distinguish, however, that here these currents do not significantly involve sodium or potassium. Further experiments are required to determine whether or not the increased inward current in low divalent ions is due to chloride.

For outward current 1/3 external potassium did not alter the leakage while low external divalent ions increased it. However, a fast time-constant potassium component might not be sensitive to external potassium changes.

Our conclusions are: (1) the leakage current, as defined, cannot be represented as a constant conductance and an apparent, constant, equilibrium potential; (2) the leakage current curve is not symmetrical about the resting (or zero) potential; (3) the time-constant of the leakage rectification is shorter than 100 μsec.; (4) only a small fraction of the leakage current can be accounted for by the inward movement of potassium, chloride or sodium ions;

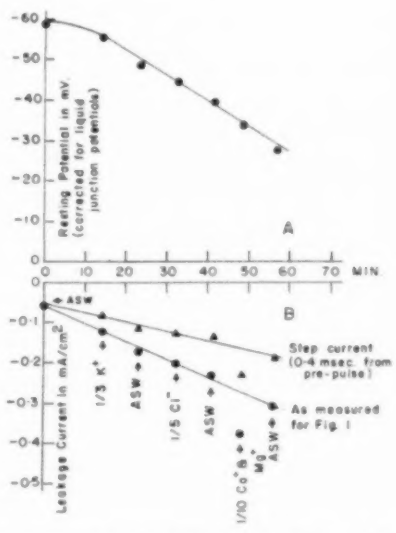

Fig. 2. *A*, Resting membrane potential versus time. *B*, Leakage current at − 180 mV. (lower curve) and this current minus that at the end of the pre-pulse (upper curve) for variations in external potassium (1/3 *N*), external chloride (1/5 *N*) and external calcium and magnesium (1/10 *N*). Temperature, 10°C.

(5) lowering external divalent ions increases the leakage; (6) the chloride conductance of the resting membrane is probably negligible; and (7) it is necessary to suppose that the leakage is mainly the outward movement of so far unidentified internal ions—cations for outward and anions for inward current components. If the properties of the axon membrane were altered so that a large fraction of membrane current had properties of the leakage current discussed here, empirical utilization of conductances and equilibrium potentials, which has been so successful for the normal squid axon, might prove impracticable.

We wish to thank Dr. K. S. Cole, Dr. U. Kishimoto, Dr. W. K. Chandler and Mr. L. Binstock for helping us.

[1] Hodgkin, A. L., and Huxley, A. F., *J. Physiol.*, **116**, 473 (1952).
[2] Cole, K. S., and Moore, J. W., *J. Gen. Physiol.*, **44**, 123 (1960).
[3] Cole, K. S., and Moore, J. W., *Biophys. J.*, **1**, 1 (1960).

REPLACEMENT OF THE PROTOPLASM OF A GIANT NERVE FIBRE WITH ARTIFICIAL SOLUTIONS

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SINCE the action potential of a nerve fibre almost certainly arises at the surface membrane, it should, in principle, be possible to replace the axoplasm by an aqueous solution of appropriate composition. The difficulty in carrying out this experiment is that the axoplasm of squid nerve fibres is a gel and is not easily washed out of an intact fibre. The method described here depends on the observation that the giant nerve fibres of *Loligo forbesi* retain their ability to propagate action potentials after the axoplasm has been squeezed out and replaced either with natural axoplasm or with an artificial solution[1]. Fig. 1 illustrates the replacement with natural axoplasm. Record *A* shows the action potential recorded with external electrodes from the central half of an intact axon. In *B*, the axoplasm from the central half had been extruded; the action potential was still present, but as a result of the increase in the internal electrical resistance, it was propagated more slowly and the component recorded with external electrodes was greatly reduced. On moving axoplasm from the distal to the central part of the fibre, the external action potential was restored to its original amplitude (*C*) and was still the same size 2 hr. later (*D*). Such experiments showed that the excitable properties of the membrane are not destroyed by extrusion and encouraged us to attempt the replacement of the axoplasm with artificial solutions.

The procedure for perfusing an axon consisted in: (1) dissecting, but not cleaning, 6–10 cm. of a fibre 500–900μ in diameter; (2) cannulating the axon at its distal end; (3) squeezing out axoplasm[2] by stroking the fibre in a series of sweeps, the first sweep starting at a distance of 2 cm. from the cut end, the second at 4 cm. and so on; (4) re-inflating the fibre at a steady rate by driving in an appropriate perfusion fluid at about 6 μl./min. After re-inflation, the electrical properties of the fibre were studied with external electrodes or, in the later experiments, with an internal electrode, using the method illustrated in Fig. 2.

For the normal perfusion fluid, isotonic solutions containing salts of potassium were employed: for example, isethionate (which is present in high concentrations in the axoplasm of squid nerve[3]), sulphate, methylsulphate or chloride. As a rule the solutions contained 30 m*M* phosphate buffer, normally at *p*H 7·7, and the tonicity was adjusted after the vapour pressure had been compared with that of the sea-water used as an external medium. Short-term experiments indicated that the action potential was little changed over a range of tonicity of $\pm$ 10 per cent and a range in *p*H of 7–8·5. A hydrostatic pressure of 2–3 cm. of water was required to keep the fibre inflated. If the pressure was released, the axon shrank to about a quarter of its original volume. In the shrunken condition the velocity of conduction was reduced but the action potential recorded with an internal electrode was little changed, as would be expected from the local circuit theory. Hydrostatic pressures of 10–20 cm. of water abolished the action potential if applied for more than a few minutes, but there was often a slow recovery after the pressure had been removed.

Potassium sulphate or isethionate media were used extensively, and with these solutions there was good evidence that the electrical properties of perfused axons were similar to those of intact axons. The action potential (100–110 mV.) and resting potential

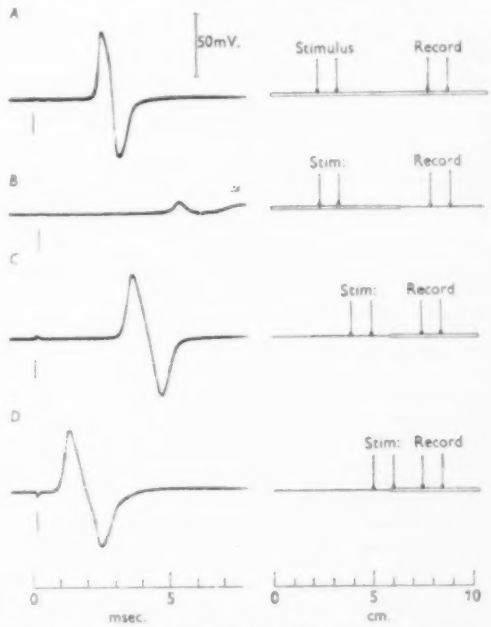

Fig. 1. Restoration of externally recorded action potential by filling 'sheath' with axoplasm. *A*, intact axon; *B*, right-hand half extruded; *C*, right-hand half filled by moving in axoplasm from left-hand half; *D*, as in *C* but 2 hr. later
A diphasic response was often observed at stage *B*, but in this experiment there was a local block between the recording electrodes which is attributed either to minor injury or to irregular flattening during extrusion

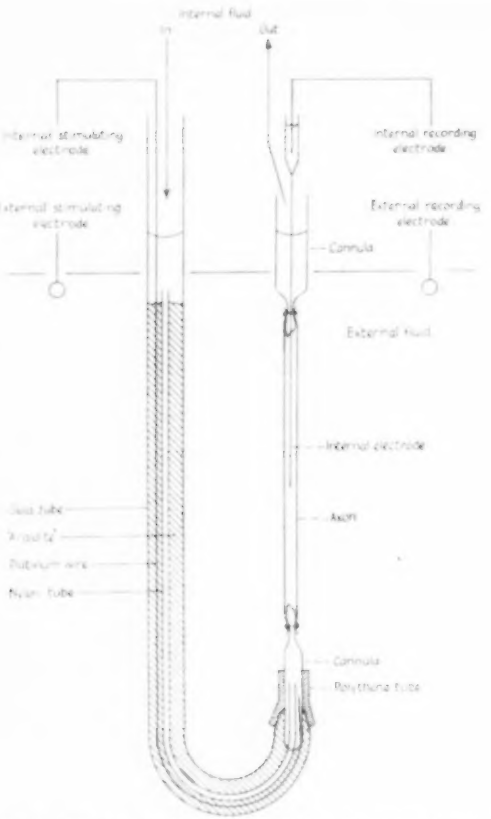

Fig. 2. Method used with internal electrodes; the drawing is not to scale

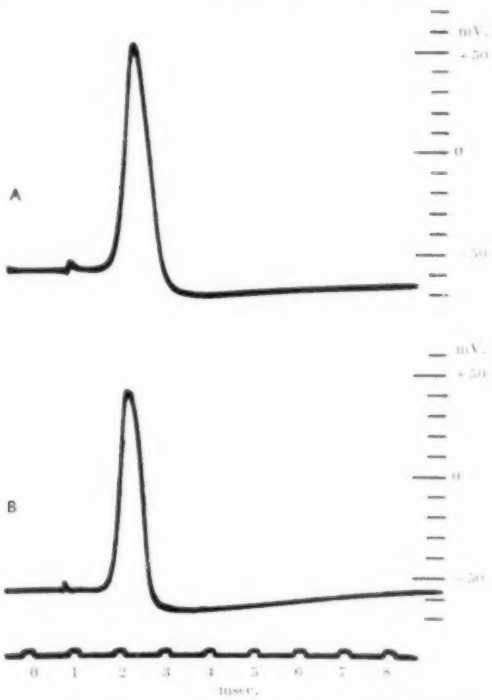

Fig. 3. *A*, action potential recorded with internal electrode from extruded axon filled with isotonic potassium sulphate (16° C.); *B*, action potential of an intact axon, with same amplification and time-scale (18° C.)
The voltage scale gives the potential of the internal electrode relative to its potential in the external solution (no correction for junction potential)

(50–70 mV.) were of the usual magnitude, and, as may be seen from Fig. 3, the time course of the action potential in a perfused axon resembled that in an intact axon. It is possible that prolonged perfusion may have some harmful effect, but a volume of 3–4 ml., which is more than one hundred times that of the fibre, could be perfused without making the fibre inexcitable. Axons filled with isotonic potassium solutions remained excitable for 3–5 hr. and were capable of carrying a large number of impulses, for example, 3×10^5 at 16° C.

Evidence that the perfusion fluid had rapid access to the surface membrane was provided by the speed with which the action potential was blocked by changing potassium for sodium ions in the perfusion fluid. With relatively short exposures, the effect of high sodium concentration was completely reversible, and both block and restoration might occur in 10–20 sec., the speed of the effect depending on the rate of flow and on the extent to which the dead space could be reduced.

Alterations in the ionic composition of the internal solution gave reversible changes in membrane potential, which were consistent with the view that the resting potential arises from the difference in concentration of potassium across a membrane which is selectively permeable to this ion[4]. Replacement of isotonic potassium sulphate with isotonic potassium chloride caused only a small decrease in resting potential, but replacement of potassium by sodium ions reduced the resting potential by about 50 mV.

Fig. 4 illustrates the effect on the resting potential of replacing potassium chloride by sodium chloride inside the axon, the external fluid being sea-water with the usual potassium concentration of 10 m*M*.

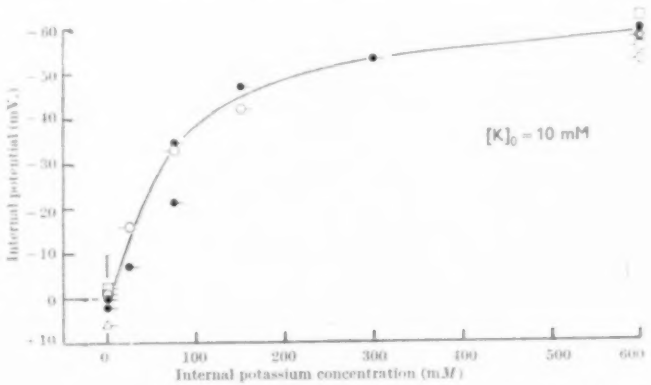

Fig. 4. Effect of internal potassium concentration on resting potential. External solution, sea-water; internal solutions, sodium chloride–potassium chloride solutions isotonic with sea-water

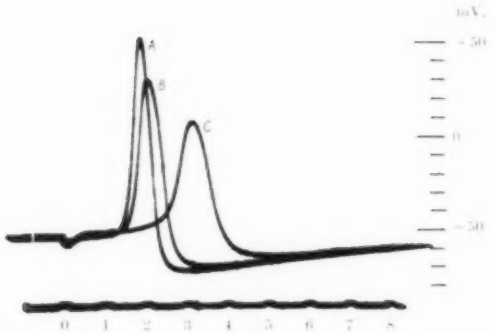

Fig. 5. Effect on action potential of replacing internal potassium with sodium ions. *A*, isotonic potassium sulphate; *B*, one quarter of the potassium ions replaced by sodium ions; *C*, half the potassium ions replaced by sodium ions. The records were taken from a long experiment and were obtained in the order *B*, *A*, *C*

With sodium chloride inside the fibre, the potential was close to zero, but it increased rapidly as potassium replaced sodium and reached a value of 40–50 mV. at an internal potassium concentration of 150 m*M*. A further rise from 150 to 600 m*M* potassium increased the resting potential by only 5–10 mV. as compared with the 35 mV. expected for a potassium electrode. This 'saturation' effect probably occurs because the permeability to potassium falls as the resting potential rises[5]. A similar hypothesis has been advanced to explain why the membrane potential ceases to behave like a potassium electrode at low external concentrations of potassium[6]. With isotonic potassium chloride outside the fibre and isotonic sodium chloride inside, the normal resting potential was reversed, the internal solution being 50–60 mV. positive to the external solution. The resting potential was close to zero if similar solutions were placed on both sides of the membrane.

The effects of varying the internal sodium concentration support the view that the action potential depends on a rise in permeability to sodium[5,7]. With sulphate as the internal anion, replacement of half the potassium by sodium caused little change in resting potential but decreased the action potential by 40–50 m*V*. Fig. 5 illustrates the effect of different concentrations of sodium ions on the action potential. From these and other records it appears that the membrane changes from a resting state, in which the permeability ratio P_{Na}/P_K is about 0·1, to an active one in which P_{Na}/P_K is 5–10.

The experiments described here raise the question of the extent to which the axoplasm is removed by extrusion and subsequent perfusion. Histological preparations showed that the volume of axoplasm in a perfused fibre was about 3 per cent of that in an intact fibre. A preliminary study of thin sections with the electron-microscope showed that the axon membrane and Schwann cell layer were present in perfused axons.

The general conclusion is that electrical changes in giant nerve fibres depend on differences of ionic concentration across the surface membrane and that the bulk of the axoplasm is not essential for the conduction of impulses.

We are indebted to Dr. J. S. Alexandrowicz for histological preparations, and to Dr. V. J. Howarth for help with the vapour-pressure measurements. Our thanks are also due to the Nuffield Foundation, the Medical Research Council, the Royal Society and the Wellcome Trust for financial support.

[1] Baker, P. F., and Shaw, T. I., *J. Mar. Biol. Assoc. U.K.*, **41** (in the press). Report for 1960–61.
[2] Bear, R. S., Schmitt, F. O., and Young, J. Z., *Proc. Roy. Soc.*, B, **123**, 520 (1937).
[3] Koechlin, B. A., *J. Biophys. Biochem. Cytol.*, **1**, 511 (1955).
[4] Bernstein, J., *Pflüg. Arch. ges. Physiol.*, **92**, 521 (1902).
[5] Hodgkin, A. L., and Huxley, A. F., *J. Physiol.*, **117**, 500 (1952).
[6] Stämpfli, R., *Ann. N.Y. Acad. Sci.*, **81**, 285 (1959).
[7] Hodgkin, A. L., and Katz, B., *J. Physiol.*, **108**, 37 (1949).

PARAPHENYLENEDIAMINE OXIDASE ACTIVITY AND COPPER-LEVELS IN MAMMALIAN PLASMAS

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THE function and properties of the blue copper-protein cæruloplasmin have been the subject of much work since it was first isolated and purified from pig and human serum by Holmberg and Laurell[1] in 1948. Cæruloplasmin is an α_2-globulin containing 0·34 per cent of copper corresponding to 8 atoms of copper per molecule. The copper is very firmly bound to the protein, is non-dialysable and does not react with sodium diethyldithiocarbamate unless it has first been liberated by denaturation of the protein. Holmberg and Laurell[2] also showed that cæruloplasmin could oxidize *in vitro* a number of substances, including ascorbic acid, catechol, adrenaline and *p*-phenylenediamine (PPD), the latter being the best substrate. This PPD oxidase activity has been adopted as the basis of a number of methods for the estimation of cæruloplasmin in serum or plasma.

The concentration of cæruloplasmin oxidase activity in the serum has been shown to vary considerably in different clinical conditions in man; it is elevated in certain acute and chronic infections and in pregnancy, while it is usually depressed in Wilson's disease. A close correlation has been demonstrated between copper-levels in plasma and oxidase activity of the plasma of man[3] and rats[4].

Gubler and co-workers[5] have differentiated two fractions of plasma copper on the basis of their reaction with sodium diethyldithiocarbamate; these fractions were designated "direct reacting copper", in which the copper reacts directly with diethyldithiocarbamate, and "indirect reacting copper" in which the copper reacts with it only after acid deproteinization of the plasma. This indirectly reacting fraction of plasma copper, which is generally assumed to correspond to the cæruloplasmin copper, accounts for a different percentage of the total plasma copper in different species. Thus this fraction in man, rat, dog and pig represents 96, 99, 88 and 56 per cent respectively of the total plasma copper[5].

The object of the present work was to determine the copper-levels in plasma in several species of mammals including man, and to find to what extent

Table 1. Comparison of the Copper Content and *p*-Phenylenediamine Oxidase Activity of the Plasma of a Number of Mammalian Species

Species	No. of samples	Total plasma copper (μgm./ml.)	*p*-Phenylenediamine oxidase activity in 0·1 ml. plasma		
			Activity/0·1 ml.	Activity/μgm. plasma total copper	Activity/μgm. indirect-reacting copper
Man*	4	1·09	0·35	0·32	0·33
Pig†	9	2·26	0·92	0·42	0·73
Sheep†	10	1·09	0·12	0·11	0·14
Cattle†	10	0·90	0·12	0·13	0·17
Dog	1	1·12	0·15	0·14	0·16
Cat†	5	0·56	0·05	0·10	0·11

Plasma copper was estimated by the method of Gubler *et al.* (ref. 6) and oxidase activity by Ravin's method (ref. 7), in which results are expressed as E(1 cm., 530 mμ). Species in which a correlation between plasma copper and oxidase activity has been observed are marked * (ref. 3). † (McCosker, unpublished work). Oxidase activity/μgm indirect-reacting copper is calculated on the basis of the percentage of indirect-reacting copper of plasma.

the *p*-phenylenediamine oxidase activity of the plasma of different species could be correlated to the indirectly reacting fraction of the plasma copper. The results, which are summarized in Table 1, show that there are considerable species differences in the total copper-levels in plasma and in the *p*-phenylenediamine oxidase activity of the plasma when this is expressed either in terms of activity/0·1 ml. plasma (as used in Ravin's test[7]) or as activity/μgm. total plasma copper. If, however, the oxidase activity is expressed as activity/μgm. indirectly reacting copper, then we find that the species differences are even more marked and are in the order pig > man > cattle, dog, sheep and cat.

It has been assumed that the oxidase activity of the plasma of the different species of mammals (Table 1) is due to cæruloplasmin for the following reasons: (*a*) the oxidase activity observed is inhibited by sodium azide, (*b*) the oxidase activity is directly correlated with copper-levels in plasma over a wide range of copper values, and (*c*) variations in the oxidase activity and copper-levels in plasma in certain species (sheep, cattle and pig) are similar to those found in man; for example, these levels are elevated in acute infections in sheep and cattle.

To explain the marked differences obtained for the *p*-phenylenediamine oxidase activities/μgm. of indirect reacting copper of the plasmas of different mammals, which are in the order pig > man > cattle, dog, sheep and cat, we may consider three hypotheses which will then be discussed in detail: (1) the cæruloplasmin copper may correspond to the whole of the indirect reacting copper fraction, the species differences being due to enzyme activators or inhibitors characteristic to the particular plasma; (2) the cæruloplasmin may be of the same standard activity, but in different concentrations in each species; (3) the differences in activity may be a result of species differences in the copper protein itself.

(1) The oxidase activity of purified cæruloplasmin is very sensitive to changes in *p*H, and to the concentrations of a number of different ions[8]. If the oxidase activity per molecule of purified cæruloplasmin were the same in all species, then the differences in activity encountered in the plasmas of various animals might be due to the presence of substances which either activate or inhibit the oxidase activity of the enzyme. Unfortunately, so far, only pig and human cæruloplasmin have been purified, and no comparative investigations of activity in terms of their copper contents have been carried out. Preliminary experiments in which the plasmas of sheep, pig and man were each dialysed extensively against water, failed to indicate the presence of any dialysable activator or inhibitor, while the oxidase activity of a mixture of equal proportions of plasma of two different species was that of the arithmetic mean of the activities of the two plasmas. The experiments therefore suggest that the activity of the enzyme in the plasma is not appreciably modified by a dialysable or non-dialysable substance characteristic of one plasma but not of the other.

(2) If the plasmas contain different concentrations of cæruloplasmin of uniform activity, then in the case of the pig, which has the highest oxidase activity observed so far, the cæruloplasmin might be assumed to account for the whole of the indirectly reacting copper fraction, whereas in man and other animals, which have a lower plasma oxidase activity, the cæruloplasmin copper would only account for a proportionally smaller percentage of the indirectly reacting copper. In these species one would have to postulate another copper-containing substance to account for the remainder of the indirect-reacting copper. As major changes in copper-levels in plasma under various physiological and pathological conditions are accompanied by proportional changes in *p*-phenylenediamine oxidase activity, this second copper-containing substance would have to change in concentration in the plasma at the same time and to the same extent as cæruloplasmin.

In the course of the purification of human cæruloplasmin by chromatographic methods, Curzon and Vallet[9] obtained a second protein peak with PPD oxidase activity. This fraction, which contained about 5 per cent of the eluted protein but only 2–3 per cent of the oxidase activity, was considered by them to be either "an active artefact" or a modified form of cæruloplasmin where the oxidase activity/protein ratio suggests that only half the active centres are functional. It is, however, unlikely that this small copper-containing fraction of lower activity could account for the species differences observed between the plasmas of man, pig and other animals, since in human plasma the oxidase activity/μgm. indirectly reacting copper is only about half that found in the pig, so that the second copper-containing substance postulated would have to account for about half the indirect reacting copper in man, and for an even greater proportion in other species, and yet be devoid of oxidase activity.

(3) From our present knowledge, it therefore appears that almost the whole of the indirect-reacting copper of the plasma is in the form of cæruloplasmin, and that the differences in oxidase activity observed in various animals are probably due to species differences in the copper–protein itself. That not all the 8 atoms of copper in the molecule of human cæruloplasmin have the same properties is indicated by the work of Scheinberg and Morell[10], who showed that in the presence of ascorbic acid only half the cæruloplasmin copper was exchangeable with copper-64, while Curzon[11] has shown that when human cæruloplasmin was digested with chymotrypsin, only 4 of the 8 atoms of copper became dialysable, the other 4 remaining in a core resistant to chymotrypsin.

Since, as is shown in Table 1, the PPD oxidase activity/μgm. indirect-reacting copper of the plasmas of different species which are in the order pig > man > cattle, dog, sheep and cat, bear an approx-

inate ratio to each other of 8 : 4 : 2, and considering the evidence presented here that in human ceruloplasmin 4 of the copper atoms are more labile than the rest[10,11], it is tempting to suggest that the observed differences in *p*-phenylenediamine oxidase activity in the plasma of various mammals may be a reflexion of the number of catalytically active copper atoms in the molecule of the ceruloplasmin of each species.

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[1] Holmberg, C. G., and Laurell, C. B., *Acta Chem. Scand.*, **2**, 550 (1948).
[2] Holmberg, C. G., and Laurell, C. B., *Acta Chem. Scand.*, **5**, 476 (1951).
[3] Holmberg, C. G., and Laurell, C. B., *Scand. J. Clin. Lab. Invest.*, **3**, 103 (1951).
[4] Neish, W. J. P., *Experientia*, **15**, 21 (1959).
[5] Gubler, C. J., Lahey, M. E., Cartwright, G. E., and Wintrobe, M. M., *J. Clin. Invest.*, **32**, 405 (1953).
[6] Gubler, C. J., Lahey, M. E., Ashenbrucker, H., Cartwright, G. E., and Wintrobe, M. M., *J. Biol. Chem.*, **196**, 209 (1952).
[7] Ravin, H. A., *Lancet*, i, 726 (1956).
[8] Holmberg, C. G., and Laurell, C. B., *Acta Chem. Scand.*, **5**, 921 (1951).
[9] Curzon, G., and Vallet, L., *Biochem. J.*, **74**, 279 (1960).
[10] Scheinberg, I. H., and Morell, A. G., *J. Clin. Invest.*, **36**, 1193 (1957).
[11] Curzon, G., *Proc. Roy. Soc. Med.*, **52**, 64 (1959).

PROTECTIVE ACTIVITY OF FRACTIONS OF TUBERCLE BACILLI AGAINST ISOLOGOUS TUMOURS IN MICE

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TUBERCLE bacilli and some of their crude fractions have been reported to be capable of initiating a wide range of non-specific changes in the resistance of animals to infectious diseases[1]. Such changes are frequently found to be accompanied by a general enhancement of antibody responsiveness. They have also been shown to be associated with alterations in certain physiological processes believed to be concerned with other aspects of the clearing mechanisms by which micro-organisms as well as foreign, effete, and abnormal cells are removed from the tissues.

It was, therefore, thought of interest to determine whether the moieties of the tubercle bacillus which have proved most effective in eliciting non-specific anti-microbial immunity possess any tumour-inhibitory powers. It has already been reported that intact, living tubercle bacilli of the *BCG* strain retard the progress of several non-isologous cancers in mice[2]. In order to avoid the immunological artificialities inherent in the transplantation of homologous and heterologous tissues, or even of very old isologous ones, all the tumour transplants employed here were of fairly recent, isologous source.

The mice were of the *BALB/c Crgl* and the *C*$_3$*H/Crgl* strains. The tumour tested in the former was a uterine sarcoma (*T*-66); those tested in the *C*$_3$*H* strain were two mammary carcinomas (*T*-32 and *T*-71), a hepatoma (*T*-46), and an osteogenic sarcoma (*T*-62). (The tumours are maintained in the tumour-bank of the Cancer Research Genetics Laboratory of the University of California in Berkeley; the *T* numbers refer to the tumour nomenclature used at the Laboratory.) The tubercle bacillus substances were the following: living *BCG* organisms; intact, phenol-killed and acetone-extracted *BCG*; and several methanolic extracts and their residues, obtained from the phenolized and acetone-treated bacilli. The preparation of these materials has been described elsewhere[3].

The experimental procedure was to subject groups of animals to a single intraperitoneal injection of different quantities of these substances, suspended in 0·5 c.c. saline. Control groups of saline-injected animals were included in every experiment. At different intervals after treatment, isologous tumours were transplanted subcutaneously into the animals by means of a trocar. The transplants consisted of pieces of tumour tissue approximately 0·5 mm.^{3} in size, and were placed on the right flank midway between the axilla and the last rib. Every attempt was made to ensure a maximum degree of sterility in the operation. The development of the tumours was followed by tri-weekly measurements of the two diameters evenly bisecting the palpable growths at right angles to each other.

The results obtained so far can be summarized as follows:

(1) Prophylactic effects of several types and of varying degree were exhibited by all the preparations tested, at certain dose-levels. Several of the non-living preparations were at least as effective as the living *BCG*, and in certain experimental circumstances more so.

(2) Several distinct types of protective effects were seen: an initial retardation of the onset of tumour development, followed by a normal rate of growth; a consistent reduction in the rate of growth; a total prevention of tumour development, with no traces of malignant growth found on autopsy of the animals killed several weeks or months after transplantation; a regression and disappearance of tumours after an initial period of development; an inhibition of metastatic spread; and a prolongation of life of animals which did develop massive tumours despite pre-treatment. Against some tumours only one, and against others several, of these manifestations of heightened resistance were displayed by the preparations.

(3) The dose of the materials was critical, the optimum quantities varying somewhat from one preparation to the next. On the whole, small quantities, of the order of 1·5 mgm., dry weight, or less, were most effective, thus paralleling the results obtained with these materials in protection experiments against heterologous bacterial infections. The optimum doses of the several vaccines differed somewhat *vis-à-vis* the various tumours. Excess quantities sometimes enhanced tumour development, even though the amounts were still considerably below the threshold of gross toxicity.

(4) The protection elicited by some of the preparations was as great, or greater, three months after

Table 1. Protective Effects against a Uterine Sarcoma in *BALB/c* Mice
(One-month vaccination–transplantation interval)

Vaccine	No. of mice out of 7 in which malignant isograft failed to develop*	Tumour area† average values (mm.²) of tumours in those animals which permitted tumour development, at the following intervals after transplantation (days)											
		20	22	25	27	29	32	34	36	40	42	46	48‡
Saline (control)	0	28	40	67	75	88	107	105	122	192	190	198	205
Living *BCG*	2	0	0	60	60	71	68	99	110	119	120	193	233
Phenolized *BCG*, 1 mgm.	4	0	0	25	24	32	50	99	99	99	108	144	156
Methanol extract, Batch No. 1, 1·0 mgm.	0	0	0	24	64	86	115	121	117	197	210	202	252
Methanol extract, Batch No. 2, 1·0 mgm.	1	25	31	56	75	84	96	132	172	166	170	191	247
Residue, 0·5 mgm.	6	24§	36	56	63	63	88	108	120	143	121	240	256
Residue, 1·0 mgm.	0	0	28	104	166	176	216	251	253	383	440§		

* No tumour found at autopsy 48–50 days after transplantation.
† Product of bisecting diameters.
‡ Tumours grossly necrotic, experiment terminated.
§ Tumour in only one animal of this group.

treatment as it was when only 2–4 weeks elapsed between vaccination and transplantation.

The results of four representative experiments are briefly shown here, in order to illustrate some of these findings:

Experiment 1. Groups of 7 *BALB/c* mice each were injected with one of the following substances: saline; living *BCG* grown for 7 days in liquid culture and then diluted ten-fold; 1·0 mgm. phenolized *BCG*; 1·0 mgm. of a methanolic extract obtained by extracting the organisms for 32 hr. (batch No. 1); 1·0 mgm. of an extract which went into the solvent between the 32nd and 82nd hr. of continuous extraction (batch No. 2); and 0·5 and 1·0 mgm., respectively, of a preparation of the exhaustively extracted residue. All animals received isotransplants of uterine sarcoma *T*·66 one month after vaccination. The number of animals which developed tumours, and the rate of growth of the cancers, are shown in Table 1.

Experiment 2. Groups of 10 C_3H mice each were vaccinated with the same materials described in Experiment 1. Isotransplantation with mammary carcinoma *T*·32 was performed one month later. The transplanted tumours grew in every animal, but differences were observed from group to group in the rate of growth. These are presented in Table 2.

Table 2. Protective Effects against a Mammary Carcinoma in C_3H-Mice
(One-month vaccination–transplantation interval)

Vaccine	Average tumour area* (mm.²) at the following intervals after transplantation (days)						
	11	13	15	18	20	22	25†
Saline (control)	102	130	256	279	369†	—	—
Living *BCG*	32	59	75	119	120	148	207
Phenolized *BCG* 1·0 mgm.	89	122	196	251	319	332	383
Methanol extract Batch No. 1, 1·0 mgm.	32	48	73	107	156	139†	—
Methanol extract Batch No. 2, 1·0 mgm.	90	139	174	241	277	317	402
Residue, 0·5 mgm.	34	52	68	102	112	115†	—
Residue, 1·0 mgm.	62	105	168	225	232	267†	—

* Product of bisecting diameters.
† Tumours grossly necrotic, experiment terminated.

Experiment 3. Groups of 8–10 *BALB/c* mice each were injected with saline; a 1 : 50 dilution of a living, 7-day-old liquid medium culture of *BCG*; or 1·5 mgm. phenolized *BCG*. Uterine sarcoma *T*·66 was transplanted into all animals three months later. It was found that the tumours placed into some of the animals regressed spontaneously after an initial period of development, while those of others progressed unchecked. These observations are illustrated in Table 3.

Experiment 4. Groups of 10 C_3H mice each received one of the following preparations: saline; 10-day-old living *BCG*, grown in liquid medium and then diluted 1 : 10; and 0·25 and 0·5 mgm., respectively, of the residue of a methanolic extraction. Four weeks later, isotransplants of osteogenic sarcoma *T*·62 were placed into the animals. The transplants grew progressively in most of the animals, but there were considerable differences in survival-time after transplantation. These are tabulated in Table 4.

These and related findings, as well as the observation that certain fractions of the tubercle bacillus possess the ability of retarding the development of already established cancers in mice, will be reported in detail elsewhere. It might be added that the protective activities of bacillary fractions against malignant tumours may bear some relation to the occasionally reported clinical and laboratory impressions that episodes of certain infectious diseases may have a beneficial influence on already-established cancers, or may reduce the likelihood of then cancer-free individuals developing neoplastic disease after recovery from the infection.

The present findings may also have some relevance for the more fundamental problem of why spontaneously arising tumours are able to grow progressively

Table 3. Protective Effects against a Uterine Sarcoma in *BALB/c* Mice
(Three-months vaccination–transplantation interval)

Vaccine	No. of animals per group	No. of animals with palpable tumours at the following intervals after transplantation (days)										98
		4	10	16	22	28	34	40	46	54	60	
Saline	10	5	9	10	10	10	10	10	10	10	10	All have massive tumours; 5 dead
Living *BCG*	8	6	8	8	7	7	7	7	7	7	7	1 alive, tumour-free; 7 have massive tumours, of which 4 dead
Phenolized *BCG*, 1·5 mgm.	9	4	7	8	8	6	4	3	3	2	2	7 alive, tumour-free; 2 have massive tumours, dead

Table 4. Protective Effects against an Osteogenic Sarcoma in *C3H* Mice

(Four-weeks vaccination–transplantation interval)

Vaccine	Cumulative number of animals dead* at the following intervals after transplantation (days)						No. of animals free of tumours at autopsy upon termination of experiment on ninetieth day
	45	55	65	75	85	90†	
Saline	0	0	0	2	6	7	1 of 3
Living *BCG*	0	1	3	3	5	7	0 of 3
Residue, 0·25 mgm.	0	0	0	0	2	4	4 of 6
Residue, 0·5 mgm.	0	0	0	0	0	0	3 of 10

* All animals dying before termination of experiment had massive tumours.

† Experiment termination.

in some individuals but not in others. Many aspects of the behaviour of malignant tumours in man and in experimental animals are consistent with the assumption that the ability of malignant cells to grow progressively in the animal body reflects a failure of the antibody or hypersensitivity-forming mechanisms, or of the phagocytic abilities of the reticulo-endothelial system[4]. Indeed, the idea has been advanced that the function of the homograft reaction is, primarily, to prevent the colonization of neoplastic cells in the normal individual[5]. Some support for this provocative suggestion comes from the clinical observations that individuals suffering from cancerous diseases show a poor ability to respond with hypersensitivity reactions to unrelated antigenic stimuli[6].

The firm establishment of an immunological theory of progressive malignancy depends, however, on the demonstration that the changes which cells undergo in the transition from normality to malignancy are accompanied by the acquisition of one or more new antigenic determinants. Largely because of the considerable technical difficulties encountered, this has not yet been shown unequivocally. It is possible, nevertheless, to secure further support for the immunological nature of the native defences against neoplastic growth and dissemination by a number of indirect approaches. The results of the present work might be taken to provide some such circumstantial evidence: If progressive neoplastic disease is, in fact, a manifestation of immunological deficiencies, it would be expected that substances which enhance both antibody production and the efficiency of the foreign body clearing reactions will also increase resistance to the development of malignant tumours. It appears that this expectation has been realized in the tumour systems which were the subject of this investigation.

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[1] Shibi, M., in *Ann. Rev. Microbiol.*, **13**, 255 (1959). Weiss, D. W., *Nature*, **186**, 1060 (1960).

[2] Old, L. J., Clarke, D. A., and Benacerraf, B., *Nature*, **184**, 291 (1959).

[3] Weiss, D. W., and Wells, A. Q., *Amer. Rev. Resp. Dis.*, **81**, 518; **82**, 339 (1960).

[4] Graham, J. B., and Graham, R. M., *Cancer*, **8**, 409 (1955). Stern, K., in *Reticuloendothelial Structure and Function*, edit. by Heller, J. H., 233 (Ronald Press, New York, 1960). Weiss, D. W. (to be published).

[5] Merrill, J. P., *Physiol. Rev.*, **39**, 860 (1959). Thomas, L., in *Cellular and Humoral Aspects of the Hypersensitive States*, ed. by Lawrence, H. S., 529 (Hoeber-Harper, New York, 1959).

[6] Holmgren, I., cited in leading article, *Brit. Med. J.*, ii, 297 (1917). Southam, C. M., Moore, A. E., and Rhoads, C. P., *Proc. Amer. Assoc. Cancer Res.*, **2**, 251 (1957). Fisherman, E. W., *J. Allergy*, **31**, 74 (1960).

CHOICE OF ANIMALS FOR BIO-ASSAY

IN marked contrast to earlier views, it is now generally accepted that, in naturally outbreeding organisms, F_1 hybrids between two inbred strains tend to show a lower level of phenotypic variability than do the parental inbred strains. The moral for the bio-assayist in search of uniformity of response, first pointed out by Mather[1], is that F_1 hybrids are, in general, to be preferred to inbreds. We have discussed this point in the course of a review[2] of methods of controlling variation in experimental animals.

The scope of the discussion has now been enlarged by C. K. Chai[3], who rightly points out that the variance of response is often not the only biometrical attribute which is of interest when assessing the suitability of a group of animals for bio-assay. In the case of quantitative (as opposed to all-or-none, or quantal) responses, the precision of the estimates is dependent not only on the variance, s^2, of the responses at a given dose, but also on the slope, b, of the dose-response line, which measures what Chai terms the 'sensitivity' of the animals.

This point was given quantitative expression thirty years ago by the introduction of λ, defined as s/b, as a suitable criterion for the comparison of the economic worth of various quantitative assay techniques for the estimation of a given substance. Thus for this type of assay it is not the absolute values of s and b which concern us, but their relative magnitude. The smaller the value of λ the more information will a given number of animals yield.

Chai also expounds the paradoxical, and potentially confusing, point that in 'quantal', or all-or-none assay the slope is merely an inverse reflexion of the variability of response, according to the relation $s^2 = 1/b^2$. It follows that no information on 'sensitivity' can be extracted from a quantal assay, and that the precision of the estimate is inversely related to the absolute value of b^2.

It is unfortunate that in the course of his further discussion of the question, Chai intermittently loses sight of these clear and valuable distinctions. The resulting confusion is such that the reader may gain an impression that the general superiority of F_1 hybrids over inbreds in respect of s^2 is in doubt. Such an impression is not justified by examination of the evidence presented by Chai. This falls into three main categories: (1) the results of a quantitative assay of testosterone, using the weights of seminal vesicles in castrated mice as the index of response: (2) the results of quantal assay of human chorionic gonadotrophin, using the percentage of immature

female mice with haemorrhagic ovarian follicles; and (3) a tabulation of published results concerning the responses of mice to hormones.

Response to testosterone. This assay was performed on the *C57BL/6* and *C57BR/cd* inbred strains and on the F_1 hybrids between them. Only animals were used the body-weight of which at weaning was in the range 9–12 gm. Although no doubt desirable for assay purposes, such a restriction renders the data of dubious value for a comparison of variation. As we have stated previously[2]: "Since the weight of the seminal vesicle is likely to be highly correlated with body weight, this restriction may have artificially brought the inbreds and F_1 hybrids being compared within the same range of variability".

The data given in Chai's Table 1 justify his conclusion that there are no differences between the inbreds and F_1 hybrids in sensitivity, measured as the slope, b, of the dose-response line. They do not justify the conclusion that the mice are equally suitable for use in the assay. The criterion for this is, as we have already said, the ratio s/b, where s^2 is the variance of response at a given dose. The relevant comparison cannot be made accurately from Chai's Table 1, since a scale has been used which makes the variances within each group grossly dependent on the value of the mean. However, inspection of the values suggests that s^2, and therefore λ also, would prove to be less for the F_1's than for the inbreds.

The hybrid mice would, therefore, be more efficient than the inbreds for the assay of testosterone. Chai reproduces in his Fig. 2 dose-response curves for another pair of inbred strains and their F_1 hybrids from an earlier publication on the same assay. Unfortunately, even from his published numerical data it is impossible to estimate λ; and the statistical manipulation of the data by which he obtained Fig. 2 is totally misleading, since λ must be computed in the scale in which the validity requirements are satisfied.

Response to chorionic gonadotrophins. In assessing the results of this experiment, we shall follow Chai's textual statement that the dependent variate was the percentage of animals with haemorrhagic ovarian follicles, and not, as stated in the legend to Table 2, the percentage of follicles. The assay is quantal, and consequently irrelevant to the context in which Chai places it, namely, differences in sensitivity. As will be recalled, in contrast to the case of quantitative assay, the slope of the dose-response line in a quantal assay yields no information on sensitivity, but is an inverse measure of variability. Interpreting in this sense Chai's values for b, we find a four-fold difference in variance between the two parental inbred strains, with the F_1 closely resembling the less variable of the two. For all five groups of mice used, the values of the slopes are very low (0·62–1·27), and although the crucial information on their standard errors is not given, it seems likely that the five estimates of slope are not, in fact, significantly different.

Tabulation of published assay results. Chai's compilation is stated to refer to "sensitivity or magnitude of response", the latter being a measure of sensitivity on the assumption that the dose-response line passes through the origin. Several quantal assays appear in his Table 2, although, as has been stated, such assays yield no information on sensitivity. (The results of Claringbold and Biggers shown in Chai's Table 2 are only partially quoted, some in error. They compared both œstrone and œstradiol-3 : 17β (not œstrone-3 : 17β, an impossible compound) by both intravaginal and subcutaneous routes of administration. Only half these results are quoted—œstrone (intravaginal) and œstradiol-3 : 17β (subcutaneous)—and in the line incorrectly labelled œstrone-3 : 17β one inbred strain (*C57*) is omitted.) If we omit the quantal assays, and further confine our attention to relevant comparisons (that is, between F_1's and their parental strains), we are left with thirteen cases. In seven the hybrids are intermediate in "sensitivity or magnitude of response", in two they resemble the superior of the two parental strains and in four they are superior to both parental strains. Surprisingly, Chai bases on this result the generalization that "F_1 hybrids are not, in general, preferable to inbred mice in hormone assay in so far as the b value is concerned". A more illuminating formulation might be that, since they are apparently not inferior in this respect (and may even prove, on average, to be superior), their known tendency towards lower variability justifies the conclusion of earlier writers that F_1's are, as a rule, preferable to inbreds for bio-assay.

It is likewise indisputable that, "For the assay of a given substance, the choice of assay animal—either an inbred or an F_1 hybrid—cannot be made in advance; it has to be based either on existing data or determined experimentally". But our contention has been, and is now, that existing data sufficiently establish a generalization which can serve as a useful, although by no means an absolute, guide to the choice of experimental material. Chai's emphasis on the empirical approach is very welcome. It does not, however, gain in effectiveness if the known facts in this field are made to appear more arbitrary and unaccountable than they really are.

A word remains to be said about the position of random-bred animals. In 1939, Emmens showed that a random-bred colony of mice was less variable in response to œstrogen than an inbred strain (Strong's *CBA*). (He did not show, as Chai reports, "that some F_1 hybrid mice were less variable in response to œstrogen than their inbred parental strains".) Other relevant tests on random-bred animals are listed in our review. Chai misquotes us as concluding that random-bred strains are more uniform than inbreds. Our actual statement[2] was ". . . unlike the comparison with F_1 hybrids, no general law can be asserted on the comparison of inbred strains with random-bred stocks". This still holds to-day. Moreover, even in animal colonies primarily concerned with bio-assay, uniformity and sensitivity are not the only criteria that matter. If a 'mouse efficiency unit' were defined so as to include the economics of fecundity, viability and growth, there are many bio-assays for which a healthy and prolific random-bred strain might provide the most economical answer.

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[1] Mather, K., *Analyst*, **71**, 407 (1946).
[2] Biggers, J. D., McLaren, Anne, and Michie, D., *Nature*, **182**, 77 (1958).
[3] Chai, C. K., *Nature*, **185**, 514 (1960).

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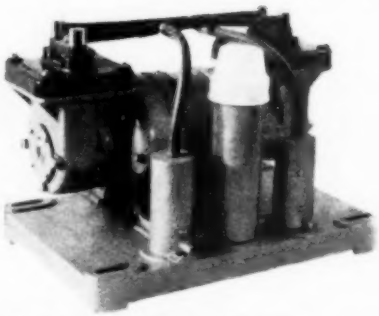

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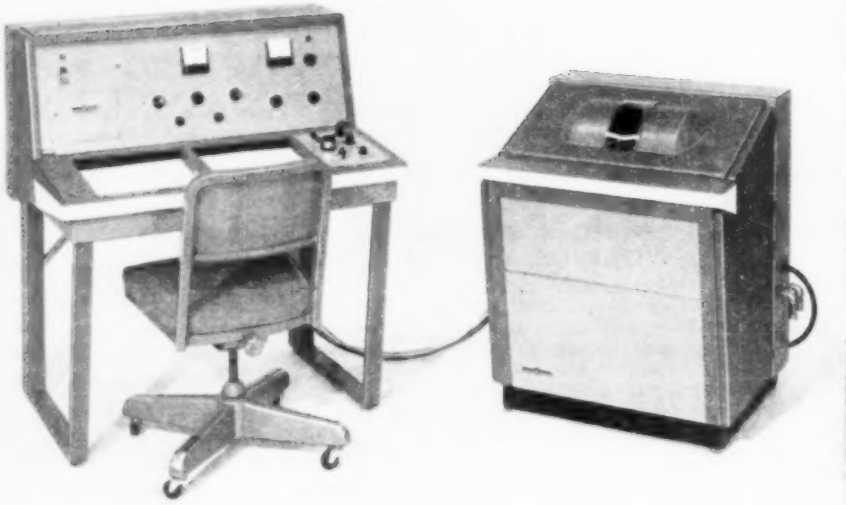

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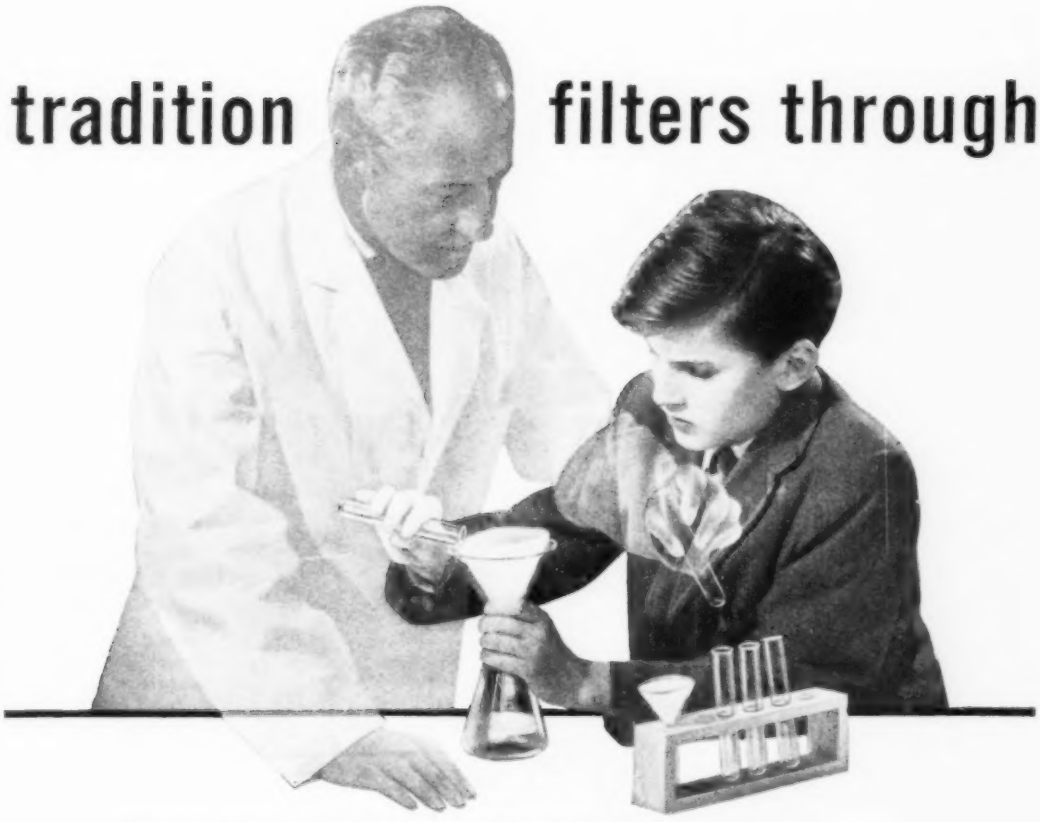

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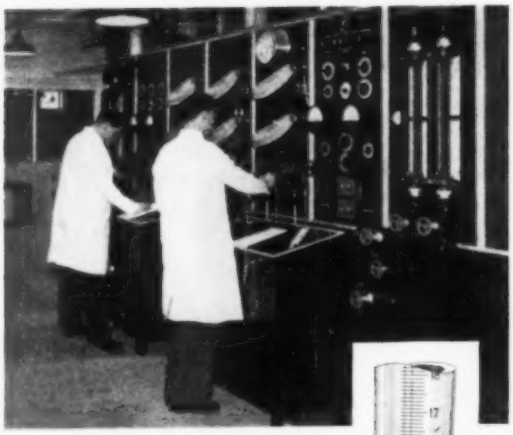

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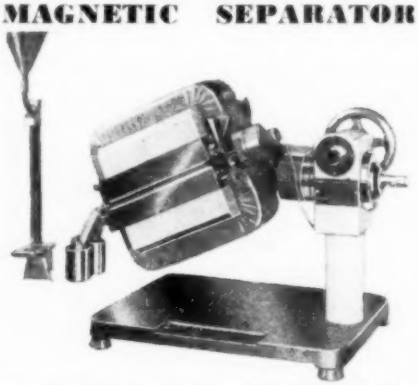

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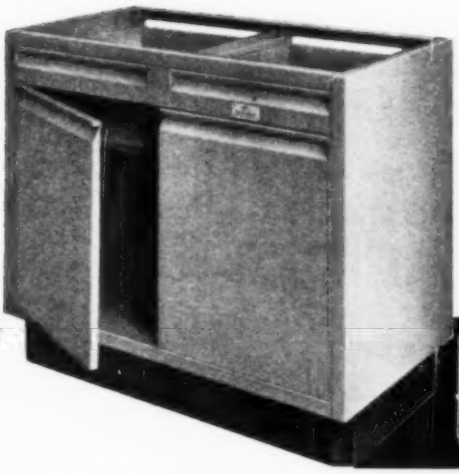

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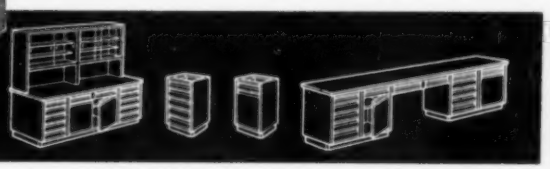

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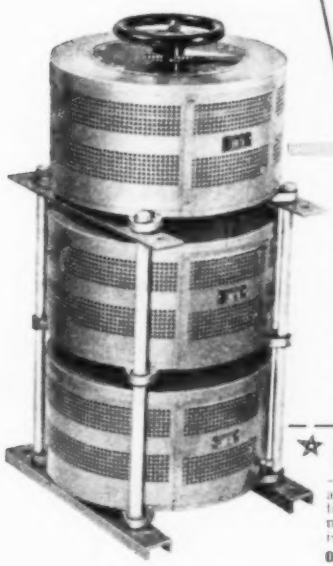

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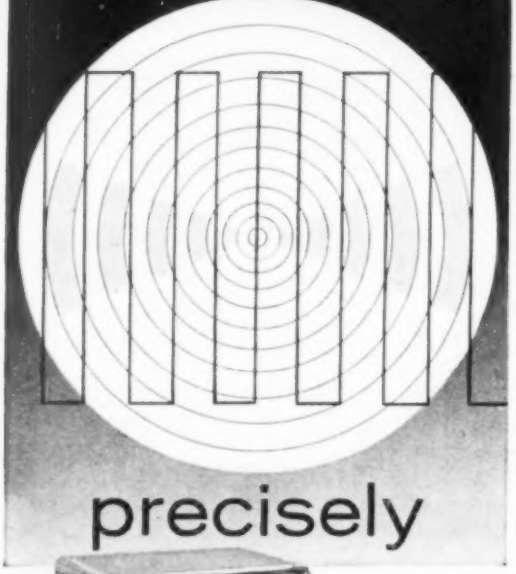

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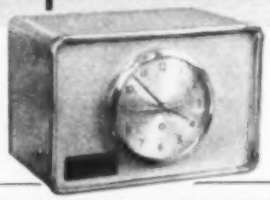

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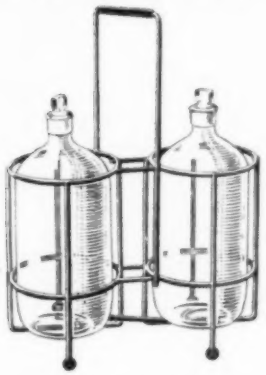

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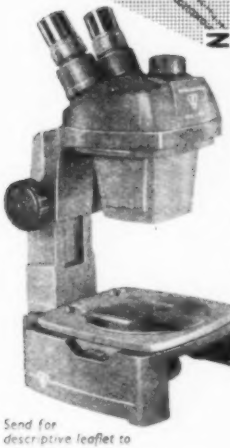

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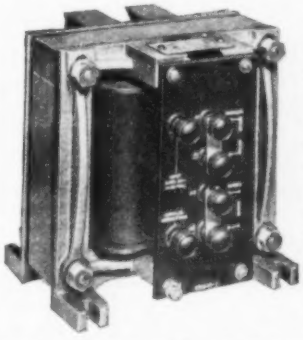

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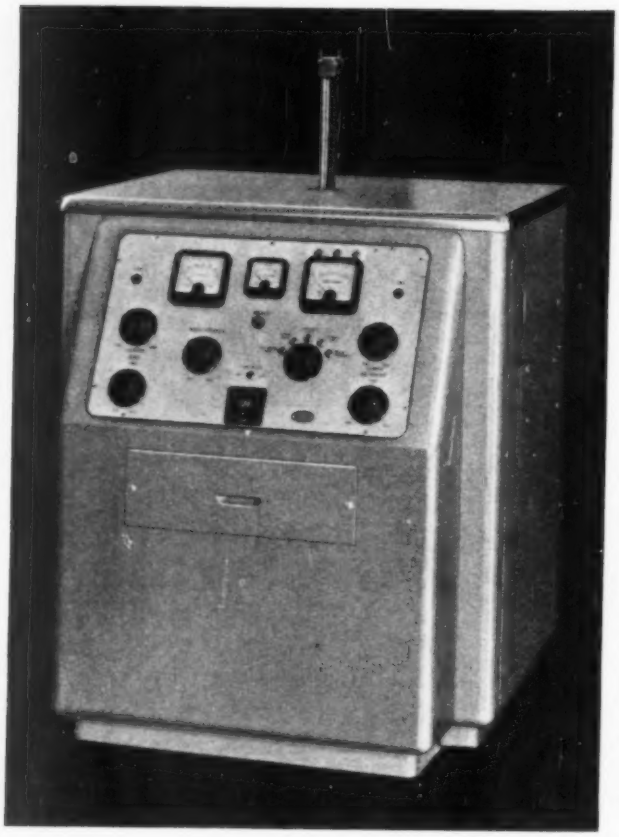

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Drs. J. D. Biggers, A. McLaren and D. Michie have commented on my article, "Response of Inbred and F_1 Hybrid Mice to Hormones", published in *Nature* of February 20, p. 514. The first of their comments supports my view that, in evaluating information of an animal in quantitative bio-assay, the slope of the dose-response curve needs to be considered. Some of their other comments, however, seem to be not much concerned with a choice between inbred and F_1 hybrid animals in bio-assay. Although I do not believe that clarification of the points which they have criticized will contribute much to the real issue at hand, I wish to make a brief defence of my position on these points. Following this I will discuss the unjustification of their conclusions.

Sensitivity. I have applied the basic principles determining the best measure of response in bio-assay as they were outlined by Gaddum and fully illustrated later by other biometricians in evaluating the bio-assay information obtainable in an animal experiment. It is necessary to draw a clear distinction between quantal and quantitative assays in terms of the importance of b. The papers published by Drs. Biggers, McLaren and Michie concerning information of an assay animal have been merely concerned with variation, and I do not think there is any need for them to restate the history of the statistics concerned. The qualitative experimental assays given in my article apply to the variance based on the relationship of $b^2 = 1/s^2$. I purposely avoided a discussion of variation in such assays and considered mainly the sensitivity measured by the slope of the dose-response curve. I do not believe that my presentation in this manner has caused confusion to readers. It may appear to be confusing to Biggers *et al.* because they have the impression that inbreds are more variable than F_1 hybrids in biological responses.

Androgen experiments. My presentation of the testosterone experiments was mainly to illustrate the point that the F_1 hybrids are not 'necessarily' more sensitive than inbreds as measured by the slope of the response curve. It is likely, when the sensitivity values of the parents differ widely, that the value of the F_1 hybrid will fall between them because of additive effects of polygenes. When the values of the parental strains are similar in sensitivity to a given stimulus, the values of the F_1 hybrids may be either greater, smaller or similar to the parental strains, depending on the degree of dominance, genic and gene-environment interactions. I used the *BALB/c*, *A Jax* experimental results to illustrate the former case and the experiment with *C57* strains to illustrate the latter. I had no intention of concluding that inbreds or F_1 hybrids were more sensitive one than the other, but rather wished to give a possible interpretation of the results based on the polygenic theory of inheritance.

I did not transform the response to render the variance independent of the means as I was not concerned with variation, but simply gave the actual means and variances for the sole purpose of plotting the means. Crude as my method may have been, I think I illustrated my point by comparing the slopes. In the experiment using *BALB/c* and *A Jax* mice, I tried many different transformations of the responses; the logarithmic transformation gave the best results although it was not fully satisfactory. Finney, in his *Statistical Method in Biological Assay*, p. 76, has pointed out that "In practice, slight heterogeneity of variance will not affect the statistical analysis very much, and a transformation that is approximately correct will be adequate . . .". In concordance with this statement, I used only the means in the comparison of bio-assay information between the inbred and hybrid mice. Also, there were no indications, from glancing at the variances, that the F_1 hybrids were less variable than the inbreds.

I judge from their criticism of my use of mice within a limited range of body-weights that Drs. Biggers, McLaren and Michie have confused 'normal variation' with 'variation in response to stimulus'. I used mice within a given range of body-weight as an aid in adjusting dosage of hormone, and to eliminate the need for correcting for differences of body-weight in the analysis of the data. Should the smaller variation in response of the F_1 hybrids be due merely to their being more uniform in body-weight, the increased variance in response could be corrected statistically. It is more likely that the differences in variation, if any, are a reflexion of physiological regulating abilities, which are, in turn, a reflexion of genetic-environment interaction.

Gonadotropin experiment and tabulations of published results. The comments concerning my experiment on response to gonadotropin and my tabulation of published data do not contradict my interpretation and conclusion that F_1 hybrids are not 'necessarily' more sensitive than inbreds. Furthermore, there seems to be no theoretical basis for them to be so.

It is mentioned that I quoted only half the results of Claringbold and Biggers. I did this because, in both their methods of administration of œstrogen, the relative order of response of inbred and F_1 hybrids was the same. I did mis-state Emmens's conclusions, and appreciate Drs. Biggers, McLaren and Michie's correction. However, I neither misquote nor mis-state the conclusion of Drs. McLaren and Michie, who have stated: " . . . On the contrary, the published facts suggest that inbred strains are usually more variable than inter-strain hybrids, with random-bred colonies occupying an intermediate position" (*J. Genetics*, **54**, No. 3, p. 454). This obviously means that random-bred animals are less variable than inbreds. Dr. Biggers *et al.* pointed out that the name of the œstrogen was incorrectly cited from their paper and the title of Table 2 of my communication published in *Nature* was not clear. I sincerely regret this carelessness.

Unjustification. Drs. Biggers, McLaren and Michie draw their conclusions without considering the importance of the 'slope' of the dose-response curve in quantitative assay; they relied on 'variation' alone. They cited thirteen papers (*Nature*, **182**, 77; 1958), including experiments using such animals as mouse, fowl and *Drosophila* for making comparisons between F_1 hybrids and inbreds. Among these thirteen papers only three dealt with biological responses: one, my paper on response to androgen, one by McLaren and Michie on the response to 'Nembutal', and the other by Claringbold and Biggers on the response to œstrogen. I have discussed my paper above and omit further discussion of it here. In the 'Nembutal' experiments (McLaren, A., and Michie, D., *J. Genetics*, **54**, 440; 1956) the authors tested inbreds, F_1 hybrids and 'Mousery' mice (random-bred) by giving the drug to the same mice on days 1, 2, 3, 8, 9 and 10, and to 'fresh mice' on day 10. They observed the response each day, but only day 1 and day 10 'fresh mice' data were used for analysis.

The remaining five days records were omitted from analysis. I calculated the variances using the data which they excluded and found the combined variances (with the degrees of freedom in parentheses) to be: 0·0346 (45) for *C57BL*; 0·0849 (43) for *C3H*; 0·0396 (44) for the F_1 hybrid; and 0·0213 (44) for 'Mousery' animals. The variance for the F_1 hybrid is smaller than that for the *C3H* strain, but greater than that for *C57BL*, although not statistically significant. The variance for the 'Mousery' mice appears to be the smallest among them. The relative order is obviously different from that which they obtained (estimate of variance: 0·0552 for *C57BL*; 0·0778 for *C3H*; 0·0165 for F_1 hybrids; and 0·0176 for 'Mousery') based on two-days records. However, perhaps their selection of data was due to their lack of understanding of the biological nature of the experiment.

The other ten papers cited by Biggers, McLaren and Michie dealt with normal variation and not with variation of biological responses. Such data might be a basis for speculation, but could not be 'definitive' evidence for conclusions about biological responses. There seems to be a lack of distinction between normal variation and biological response.

It is clear that at the present time no one has sufficient amounts of critical evidence for the generalization which these investigators have made. It is true that Mather suggested the possibility of using F_1 hybrids in bio-assay, and Lerner pointed out that heterozygotes have better self-regulating ability than homozygotes. Moreover, I believe that under ordinary environmental conditions and without treatment, the F_1 hybrids may be more homogeneous in morphological traits than inbreds, but to equate this morphological homogeneity with response to chemical or biological stimuli requires further experimental evidence.

It is well established that there are species differences in sensitivity and that, in bio-assay, preference is given to certain species for certain assays; for example, metamorphosis in the tadpole for assay of thyroid hormone; comb-growth of chicken for androgen; crop-gland secretion of pigeon for lactogenic hormone; and uterus growth in mice for oestrogen. I believe that there are differences also in sensitivity between races, breeds and strains within species as well. Indeed, some differences have been shown to exist between mouse strains, as already illustrated in my article in *Nature*, **185**, 514; 1960. Inbred strains can be very useful for assays of certain substances. This has been well illustrated and discussed by Becker and Berg (*Poultry Sci.*, **38**, 362) in a paper in which they compared inbred and hybrid chickens in high and low planes of nutrition.

Finally, I reiterate that I do not underestimate the potentiality of F_1 hybrids for use in bio-assays. It has been claimed that the heterozygotes are better 'buffered' than the homozygotes, but differences between them in the mechanisms of reactivity are poorly understood. Our understanding of genetic pathways in the polygenic systems are practically nil, and reliable data from comparisons in bio-assay values between inbreds and F_1 hybrids are limited. Assay substances from synthetic and biological sources are numerous, and their end-points in assay vary widely from physiological and morphological measurements to rates of survival. In these circumstances, it seems wise to use an empirical approach, as I have, rather than to draw conclusions which might mislead the experimenter into believing that there is more evidence available for his making a choice of animal material than actually exists.

C. K. Chai

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Dr. Chai has now raised a criticism of an earlier paper of ours (*J. Genet.*, **54**, 440; 1956). As explained in the paper in question, estimates of variance of response derived from animals which have acquired a degree of resistance through previous exposure to the drug have no simple interpretation. Our "selection of data" consisted of using only estimates of variance derived from mice not previously exposed to the drug. Furthermore, it is not statistically legitimate to pool variance estimates, as Chai has done, when the estimates are derived from the same mice on different occasions and when the responses on different occasions are correlated. As for Chai's distinction between "variation of biological responses" and "normal variation", in so far as these two categories can usefully be distinguished, it is not easy to see why they should not be subject to the same underlying mechanisms of genetic and developmental homeostasis. We have discussed these matters more fully elsewhere (*New Biol.*, **19**, 48; 1955).

Anne McLaren

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Development of resistance to drugs, particularly those affecting the central nervous system, is well known. The analysis which Drs. McLaren and Michie made, testing the significance of this, was not convincing, for their interpretation (that response to 'Nembutal' is affected by previous dose) was based on only part of their results. The primary concern in pooling or comparing variances of different groups should be that the variance is independent of the mean, not that there was, or was not, previous exposure to the drug. McLaren and Michie used the logarithmic scale for correcting the dependence of the variance on the mean. This transformation was not adequate, as they themselves stated, ". . . this applies too strong a correction and results in a negative correlation between variance and mean". When I analysed their results, I noticed that they pooled the variance-estimate in the two-day tests and compared the variances without considering that the means were different and the transformation not adequate. Transformation of data for biological responses is often a troublesome matter and it is difficult to obtain an adequate scale. I reiterate that although "variation of biological response" and "normal variation" may be subject to the same underlying genetic and developmental mechanisms, further experimental evidence is necessary before this can be accepted as fact. Furthermore, there is little information available regarding differences in variability between inbred and F_1 hybrids in characters which have different evolutional significance. Speculation with regard to homeostasis, a concept which is theoretical and controversial, should not be substituted for proof.

C. K. Chai

LETTERS TO THE EDITORS

ASTRONOMY

Origin of Jupiter's Great Red Spot

THE Great Red Spot in the southern hemisphere of Jupiter's otherwise ever-changing surface of dense cloud has baffled astronomers for many years[1,2]. The purpose of this communication is to outline the results of elementary dynamical and hydrodynamical considerations which suggest a straightforward explanation of the phenomenon. Contrary to generally accepted views[3], the non-uniform rotation of the Great Red Spot does *not* rule out the possibility that its origin is in the 'solid planet'; I believe that quite a shallow 'topographical feature' of the surface of the 'solid planet' could account for the observations. The theory should be amenable to further observational tests, and an experiment is now in hand to check the chief theoretical argument on which it is based.

The mean radius of Jupiter is about 70,000 km. The Great Red Spot, which is elliptical in shape, having its long axis along zenocentric latitude 22° S., occupies 30° of longitude and 10° of latitude. According to observations of the motion of markings on Jupiter's visible surface[2], which go back more than a century, the rotation of this surface about the axis of the planet is non-uniform, being a complicated function of latitude which is unsymmetrical about the equator. The period of rotation of the equatorial zone is 5 min. less than that of other regions, and astronomers find it convenient to refer to the more rapidly rotating part of the disk as System I and the other parts as System II. Their average periods with respect to position and time are, respectively, 9h. 50m. 30s. and 9h. 55m. 40s. In System II, spatial variations of the mean period with respect to time range from 9h. 55m. 5s. to 9h. 55m. 54s. As regards variations in time of the rotation periods in System II, these are erratic and have a range from ±5 sec. to ±10 sec. depending on position on the disk. Within System I, the equatorial zone, the rotation is most rapid roughly on the equator itself. Temporal fluctuations in period over a range ±15 sec. are indicated by the observations.

During the past hundred years or so, the period of the Great Red Spot has varied between 9h. 55m. 31s. and 9h. 55m. 44s., the average value being 9h. 55m. 38s.; the corresponding amplitude of this drift in longitude with respect to the mean motion is 1,080°, and on the present hypothesis the motion of the Spot is also that of the 'solid planet'. The average (with respect to position) period of the South Tropical Zone, in which the Spot is embedded, has varied between 9h. 55m. 27s. and 9h. 55m. 36s. The corresponding average linear velocity of the South Tropical Zone with respect to the Spot is about + 2 m./sec., the positive sign indicating that this motion is in an eastward (westerly) direction. Points on the equator rotate about the axis of the planet at 12 km./sec.

The mean density of Jupiter is 1·34 gm./cm.³. According to Wildt's theoretical model[4,5], the atmosphere has a depth d (say) of 12,000 km. and a mean density of 0·35 gm. cm.⁻³. The corresponding moment of inertia of the atmosphere about the rotation axis exceeds 0·2 of that of the whole planet. Assuming that the motions of the visible surface are representative of the flow at lower levels (and this assumption has some theoretical backing) it is possible to estimate the order of magnitude of temporal fluctuations in the angular momentum of the atmosphere. This turns out to be comparable with the fluctuations of the angular momentum of the 'solid planet' as evinced, on my hypothesis, by the motion in longitude of the Great Red Spot, and it follows therefore that transfer of angular momentum between atmosphere and 'solid planet' might account for this motion. Evidently, Jupiter's 'day' is subject to quite large variations, probably due to meteorological causes.

The variation of latitude of the Great Red Spot expected on the present model is utterly negligible, and this accords well with observation.

Hydrodynamical theory suggests that Jupiter rotates so rapidly that the effect on the general circulation of the atmosphere of quite a shallow 'topographical feature' of the 'solid planet' will be attenuated very slowly with height, and thus the 'feature' will make its presence manifest at the level of heavy cloud at the top of the atmosphere. Specifically, the atmospheric flow cannot surmount the 'feature' if h, the height of the 'feature' above (or depth below) the general level, exceeds:

$$h_c \equiv \varkappa d(U/L\,\Omega) \qquad (1)$$

where $\varkappa$ is a number of order unity, U is a characteristic wind speed in the vicinity of the 'feature', L is a typical horizontal dimension of the 'feature' and Ω is the angular speed of rotation of the solid planet. When this criterion is satisfied, there will be a stagnant column of fluid stretching, not necessarily in a vertical direction, from the 'topographical feature' at the bottom of the atmosphere all the way to the top of the atmosphere. This column of fluid will partake of the motion of the 'topographical feature' and virtually no mixing will occur between the fluid within the column and that without. Although effects of this kind were predicted and demonstrated long ago by Sir Geoffrey Taylor[6], the foregoing criterion for 'Taylor columns' to occur is only based on crude theoretical arguments of my own. The criterion is now being tested in my laboratory.

If L = 25,000 km., d = 12,000 km., U = 2 m./sec. and $\Omega = 1{\cdot}5 \times 10^{-4}$ rad./sec., according to equation (1), h_c = 6 km. Although geometrically shallow, stresses in the 'solid planet' due to the presence of a 'topographical feature' having this height would exceed 10^8 dynes/cm.². If the 'feature' cannot be supported elastically, it may be necessary to invoke slow convection in the 'solid planet' to account for it, assuming that to forces of slow period the 'solid' is really a very viscous liquid. The coefficient of viscosity of the 'solid' would then have to exceed 10^{19} gm. cm.⁻¹ sec.⁻¹.

Equation (1), which shows h_c is *inversely* proportional to L, suggests a possible explanation of the uniqueness of the Great Red Spot, for if there were no

'topographical feature' having L in excess of 40,000 km. and h nowhere substantially exceeding the critical value for the Spot, other 'topographical features' would only produce spots on those occasions when U has a sufficiently low value. This appears to be borne out by the occasional appearance of short-lived spots, slightly smaller than the more permanent Great Red Spot, and it will be of importance to scrutinize the observations more closely in this connexion. It is not permissible to apply equation (1) to very shallow 'topographical features', because then friction has to be taken into account.

Considerations of the atmospheric flow around the hypothetical column of fluid underlying the Great Red Spot account for the presence of the Red Spot Hollow[2] on the equator-ward side of the Spot and for the bizarre nature of the interaction of the Spot with the South Tropical Disturbance[2]. Atmospheric turbulence resulting from the presence of this column will be most intense on the poleward side of the column, and this may bear on the interpretation of radio astronomical observations of Jupiter[5-7]. Recently, bursts of radio noise have been reported, and the electromagnetic energy in a typical burst estimated at about 10^{18} ergs. As the kinetic energy of a typical turbulent eddy in Jupiter's atmosphere (about 10^{24} ergs) is several orders of magnitude bigger than this, one wonders whether radio bursts are due to lightning flashes associated with thunderstorm activity, or to strong interaction between this turbulence and Jupiter's ionosphere.

R. Hide

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[1] Phillips, T. E. R., article on "Jupiter" in the fourteenth edition of the *Encyclopædia Britannica* (1929).
[2] Peek, B. M., *The Planet Jupiter* (Faber and Faber, Ltd., London).
[3] Russell, H. N., Dugan, R. S., and Stewart, J. Q., *Astronomy*, I, *Solar System* (Ginn and Co., Boston, 1945).
[4] Wildt, R., *Mon. Not. Roy. Astro. Soc.*, **107**, 84 (1947).
[5] Taylor, G. I., *Proc. Roy. Soc.*, A, **104**, 213 (1923).
[6] Bracewell, R. N., ed., *Paris Symposium on Radio Astronomy* (Stanford Univ. Press, 1959).
[7] Carr, T. D., Smith, A. G., Pepple, R., and Barrow, C. H., *Astrophys. J.*, **127**, 274 (1958).
[8] Payne-Gaposchkin, C., *Introduction to Astronomy* (Eyre and Spottiswoode, London, 1956).

ASTROPHYSICS

Anomalies in the Light Curves of Meteors resulting from Fragmentation

In one of a series of papers on the physical theory of meteors, Jacchia[1] has pointed out that while the observed decelerations and light curves of bright meteors are in good agreement with the simple ballistic theory, the fainter meteors photographed with the Baker Super Schmidt cameras show startling anomalies. He has adduced evidence to show that the theory of progressive fragmentation of the meteoroid offers a simple explanation of the observed anomalies.

In a recent communication[2], I have shown that the observed light curves of a random sample of 360 meteors studied by Hawkins and Southworth[3] suggest that the luminous efficiency factor τ in the luminosity equation for meteors has to be regarded as a variable along the trail of an individual meteor and proportional to the atmospheric density ρ at every point of the trail. It was shown that the normalized light curve, when the theory is thus modified, fits better with observational data than the corresponding curve of the conventional theory. For a single-body meteoroid, if we denote by α and β the height-intervals from the level maximum luminosity (corresponding to stellar magnitude $M_{max.}$) to levels of equal luminosity (corresponding to stellar magnitude M) on the ascending and descending branches of the light curve, then the ratio $\alpha/(\alpha + \beta)$ is related to $M - M_{max.} = \Delta M$. For a given value of ΔM, the values of this ratio as given by the conventional and modified theories are nearly the same as can be seen from Table 1.

Table 1

ΔM	$\alpha/(\alpha+\beta)$		ΔM	$\alpha/(\alpha+\beta)$	
	Conventional theory	Modified theory		Conventional theory	Modified theory
0·5	0·631	0·613	4·0	0·814	0·798
1·0	0·680	0·663	4·5	0·827	0·813
1·5	0·713	0·691	5·0	0·839	0·827
2·0	0·737	0·720	6·0	0·858	0·846
2·5	0·761	0·747	7·0	0·871	0·861
3·0	0·782	0·769	8·0	0·883	0·873
3·5	0·799	0·788			

I directed attention to the fact that, according to the single-body theory, the height-interval from the level of maximum luminosity to the level of complete ablation is independent of the mass of the meteoroid and is uniquely related to the scale-height a of the atmosphere, being equal to $1{\cdot}1a$ according to the conventional theory and $0{\cdot}7a$ according to the modified theory. The effect of fragmentation on the light curve is, in general, to shorten the ascending part of the curve (α), and, in a good many cases, to lengthen the descending part of the curve (β). Without going into details, it may be mentioned that the ratio $\alpha/(\alpha + \beta)$ will decrease from the theoretical value as a result of fragmentation. I have therefore made use of this parameter as a rough index to study the behaviour of the 360 meteors listed by Hawkins and Southworth. The value of the ratio is found to be less than 0·6 for nearly two-thirds of the meteors. Rejecting these, the values of α and β for the remaining meteors are plotted in Fig. 1 against the appropriate values of ΔM. By this process of selection, I have eliminated the large majority of the fragmented meteors, so that the behaviour of the light curves of those remaining may be expected to show a close

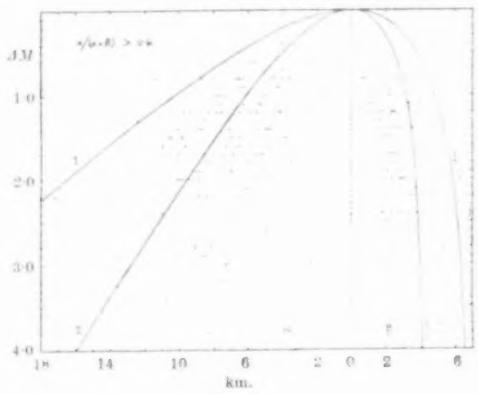

Fig. 1

degree of approximation to the theoretical light curve. Curves 1 and 2 in Fig. 1 are the normalized light curves according to the conventional and modified theories for a scale-height value of $a = 6{\cdot}38$ km. It is clearly seen that the observational data are in accord with the light curve 2 of the modified theory.

To study the behaviour of meteors brighter than those in the random sample of Hawkins and Southworth, I have examined the data of 144 meteors listed by Whipple[4]. Whereas less than 3 per cent of the meteors in the random sample had the end-points of their trails below 75 km., nearly 50 per cent of Whipple's meteors had their trails ending between 75 and 40 km. For about a third of these meteors the ratio $\alpha/(\alpha + \beta)$ was found to be less than 0·6. Rejecting these, and plotting the data of the remaining meteors in a manner similar to that of Fig. 1, it is found that the light curves of the brighter meteors too are in better conformity with the normalized light curve of the modified theory than with that of the conventional theory.

The Draconid shower meteors of October 1946 gave, for the first time, the clearest indication of the need to revise the concept of the single-body meteoroid, and to replace it with the concept of the meteoroid being 'a cluster of breaking fragments' (refs. 1 and 5). The data relating to these meteors taken from the paper of Jacchia, Kopal and Millman[6] have been plotted in Fig. 2. Comparison of Figs. 1 and 2 brings out strikingly the effect of fragmentation on the light curves of meteors.

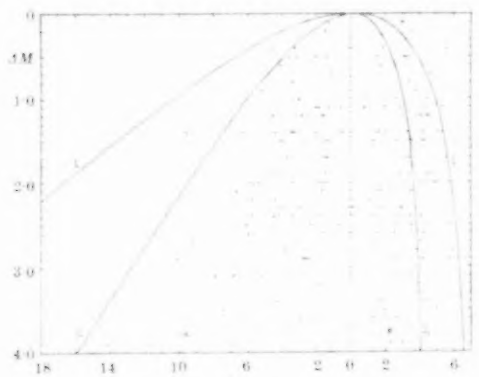

Fig. 2. Draconid shower meteors (Jacchia, Kopal and Millman)

For the luminous efficiency factor τ in the luminosity equation for meteors, Whipple derived the relation :

$$\log \tau = \log \tau_0 + \log v = -9{\cdot}07 + \log v$$

where v is velocity of the meteor in cm./sec. It is significant to note that the value of log ρ at 100 km. for the Rocket Panel Atmosphere (1952) is $-9{\cdot}065$, which is practically equal to log τ_0 in Whipple's equation. It is also of interest to note that the mean value of log ρ between 120 km. and 80 km. for the Rocket Panel Atmosphere is $-9{\cdot}02$. Whipple's equation is, therefore, very nearly equivalent to :

$$\tau = \tau_0 \bar{\rho} \sim \rho v$$

where $\bar{\rho}$ is the atmospheric density at 100 km. or the mean atmospheric density between 120 and 80 km. The observational data relating to light curves of meteors are in better accord with the relation :

$$\tau \propto \rho v$$

where ρ is a variable along the meteor trail.

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[1] Jacchia, L. G., *Astrophys. J.*, **121**, 521 (1955).
[2] Ananthakrishnan, R., *Nature*, **187**, 675 (1960).
[3] Hawkins, G. S., and Southworth, R. B., *Smith. Cont. Astrophys.*, **2**, 349 (1958).
[4] Whipple, F. L., *Rec. Mod. Phys.*, **15**, 246 (1943); *Advances in Geophysics*, **1**, 135 (Academic Press Inc., New York, 1952); *Astro. J.*, **59**, 246 (1954).
[5] Öpik, E. J., *Physics of Meteor Flight in the Atmosphere*, 149 (Interscience Publishers, Inc., New York, 1958).
[6] Jacchia, L. G., Kopal, Z., and Millman, P. M., *Astrophys. J.*, **111**, 104 (1950).

Nanometeorites

This communication is a preliminary report of our work on a high-altitude airborne particle collection obtained in the Arctic on November 15, 1960. The collector was exposed from a *U*-2 aircraft at an altitude of 60,000 ft. at longitude 144° W. and at latitudes ranging from 71° to 73° N. for a duration of 366 min.

The particle collector was of an impact type which could simultaneously expose four collection surfaces each with a different effective collection area and consequently different particle-size cut-offs. The smallest particles which could be individually collected were approximately 0·2μ in diameter. The particles were collected directly on high-purity 'Formvar' films approximately 70 Å. thick supported by 200 mesh/in. copper screening. The exposed screens were examined by electron microscopy without any chemical treatment after exposure. The moving and exposed parts of the collector were either coated with 'Teflon' or constructed from 'Teflon' to eliminate the need for lubrication for de-icing.

Examination of the exposed samples revealed enormous numbers of ultra-small, high-density particles of the order of 75 Å. in size in addition to the solid and 'fluffy' particles larger than 0·2μ normally seen in previous high-altitude collections at lower latitudes.

Fig. 1 shows an electron micrograph of a portion of a cluster of these ultra-small particles, a 0·1μ scale and unresolved background material with some holes from which very small spherical particles appear to have evaporated. Table 1 shows approximate particle-size distributions for these high-density spherical particles and for some ultra-small irregular particles which were also found.

These extremely small particles and the background material have also been studied by selected-area electron diffraction. The high-density spherical particles have given diffraction patterns indicating

Table 1

Diameter size-range (Å.)	No. of small spherical particles per size-range	No. of irregular solid particles per size-range
0–50	1,092	107
50–100	735	137
100–150	256	145
150–200	72	127
200–250	16	57
250–300	2	10
300–350	—	3
350–400	—	1

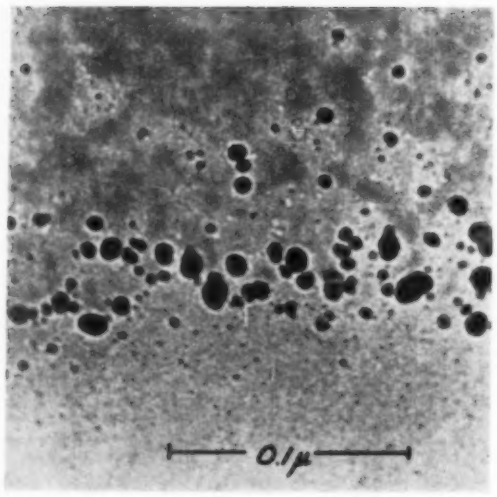

Fig. 1

compositions of nickel monoxide and also of taenite. The background material and the irregular particles appear to be partly nickel monoxide and ferric oxide.

The following additional comments concerning these ultra-small particles are appropriate:

(1) They are always found clustered, suggesting that at the altitude of collection they were within a larger particle which has afterwards evaporated, probably under electron-beam bombardment in the electron microscope.

(2) The small spherical type and the background material have been occasionally detected by us in other high-altitude aircraft collections and in balloon collections during the past four years.

(3) This collection was made during a period of unusual solar activity in the auroral zone. Major solar flares were observed on November 12 and November 15, 1960.

(4) The ultra-small particles appear to be about 100,000 times more numerous than particles 0·2μ in size or larger.

(5) The four simultaneously exposed collection areas showed an approximately correct decrease in particle numbers per unit area with an increase in collection aperture and particle-size cut-off, indicating freedom from contamination of samples.

(6) Previous high-altitude collections at lower latitudes have indicated that, at altitudes greater than 50,000 ft., one is substantially free of contamination by terrestrial particles and that numbers of particles collected are roughly proportional to duration of exposure.

We feel that the evidence is strong for the existence of a previously unsuspected class of meteoric bodies entering the Earth's atmosphere. Since these ultra-small bodies are approximately a thousand times smaller in diameter than the expected sizes of micrometeorites, and since the forces acting on them are likely to be critically dependent on their electrical charge and velocity in the Earth's ionosphere and magnetic field, we propose, for convenience, to label these ultra-small particles nanometeorites.

Nanometeorites may in part result from meteorite ablation, or meteor fragmentation. We are inclined, at present, to favour a lunar dust origin for these particles. A full report on nanometeorites will be published at a later time.

We wish to thank Mr. Herbert Cohen and Mr. Joseph Frissora, of the Space Instrumentation Division of the Technology Instruments Corporation of Acton, Mass., for the design and construction of this particle collector, and Dr. James Friend, of Isotopes, Inc., at Westwood, New Jersey, for arranging to have this collector flown for us by the Armed Forces Special Weapons Agency.

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GEOPHYSICS

Possible Identification of Atmospheric Waves associated with Ionospheric Storms

It has been noticed that ionospheric storm effects are not simultaneous at polar and more temperate regions. The purpose of this communication is to present the results of an inquiry into the nature of travel of these storms.

Mason[1] has described the general properties of night-time storms at Christchurch, and has noticed that one class of storm has relatively simple characteristics. These were storms with magnetic sudden commencement followed by easily identifiable storm features in the ionosphere. The latter were characterized by rise in virtual height of *F* layer and drop in critical frequency often accompanied by oblique echoes and enhanced *E* layer ionization. Such storms were chosen for study as they gave the least ambiguous effects.

Night-time ionograms were studied at Christchurch (43° 34′ S., 172° 48′ E.) and at Campbell Island (52° 33′ S., 169° 09′ E.) in order to measure the northward component of any travelling phenomena. Periods immediately preceding and following a local night-time magnetic sudden commencement with *K*-index disturbance of 5 or more, during July 1957–February 1961, were used. These times included the eighteen months of the International Geophysical Year, during which the standard of recording was particularly suited to the project. The criteria of an ionospheric storm were a sudden drop in the critical frequencies and a rise in virtual height of the *F* layer, and other features—oblique echoes, retardation of extraordinary ray, and night *E*—noted. The first rise in virtual height of the *F* layer was taken as the onset of the storm, though the changes in height were usually more extreme at Campbell Island than at Godley Head.

32 storms in all were studied; but for the following reasons 24 were discarded: (*a*) 7 were discarded as their onset-time was obscured by continuing effects of earlier storms; (*b*) 8 were discarded because sunrise occurred before storm onset; (*c*) 4 were discarded as onset at Campbell Island was obscured by polar cap absorption; (*d*) 5 were discarded as no storm developed at Christchurch.

The remaining 8 storms were considered sufficiently reliable to measure the apparent velocity between

Table 1. The Apparent Velocity of Storm Sudden Commencements deduced from the Ionograms

Time of storm (G.M.T.)	Maximum K-index of disturbance	K-index over considered period	Time of onset at Campbell Island (G.M.T.) Lower limit	Upper limit	Time of onset at Christchurch (G.M.T.) Lower limit	Upper limit	Apparent velocity (m./sec.) from Campbell Is. to Ch'ch. Lower limit	Upper limit
Dec. 19, 1957, 09·37	5	4	10·50	11·00	11·31	11·33	428	592
July 8, 1958, 07·50	7	6	07·58	08·00	08·38	08·40	438	485
Sept. 3, 1958, 08·42	7	4–5	08·50	09·00	09·20	09·30	460	921
Feb. 11, 1959, 07·55	6	4–6	08·40	08·50	09·20	09·30	368	613
Mar. 26, 1959, 08·42	7	4–5	09·00	09·10	09·34	09·47	392	767
Aug. 16, 1960, 14·09	6	4–5	14·42	14·55	15·17	15·30	384	837
Oct. 24, 1960, 14·54	6	5	15·17	15·30	16·02	16·15	318	575
Nov. 12, 1960, 13·50	9	5	16·05	16·15	16·40	16·45	460	737
Mean:							406	691

these two stations. With ionograms taken only at certain fixed times, the velocity may only be stated between limits. Table 1 gives the list of storms with sudden commencement times, followed by onset times at Campbell Island and Christchurch. The spherical distance between these two stations was 1,105 km. at a height of 150 km., and using these data the velocity limits were calculated.

The K-index first used was that describing the maximum disturbance period in the course of the magnetic storm, but for this work, the K-index for the actual period involved from sudden commencement until storm onset was more appropriate. These figures were more consistent with a correlation between delay time and magnetic activity, the event on July 8, 1958, having greatest activity and least delay until storm onset. As the K-index figures were only available for successive 3-hr. periods daily they are still not a sufficiently accurate measure for detailed work of this nature.

In several cases the readings from ionograms were taken from 15-min. records, giving correspondingly wider limits to the observed velocity.

It is obvious from Table 1 that the northward component of apparent velocity is well defined and, as this is also the most probable direction for any storm effects originating in the polar or auroral regions, this will be taken as the apparent velocity.

From the results it is suggested that this velocity is that of a neutral gaseous wave, being of the same order as that found for the limiting velocity of the disturbance from the Johnston Island nuclear explosion, that is, 470 m./sec. at 150 km. (ref. 2). It is further suggested that the apparent vertical movement of the ions is caused by the interaction of the ionized component of the disturbed atmosphere with the magnetic field. The dissipation of this wave would also explain the more pronounced effects at Campbell Island than at Christchurch, and also the five cases where no storm developed at Christchurch.

This work is part of the research programme of the Christchurch Geophysical Observatory, Department of Scientific and Industrial Research, New Zealand, under the superintendent, Mr. J. W. Beagley. I wish to thank Mr. C. H. Cummack for his guidance and also Mr. G. A. M. King for helpful discussions.

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[1] Mason, R. F., *N.Z. J. Geol. and Geophys.*, **1**, No. 3 (1958).
[2] Cummack, C. H., and King, G. A. M., *N.Z. J. Geol. and Geophys.*, **2**, No. 3 (1959).

GEOLOGY

Granite beneath the Northern Pennines

A fully cored borehole sited at Rookhope (*NY*35/937.428), West Durham, has proved the existence of granite at 1,281 ft. depth directly beneath Lower Carboniferous (Visean) strata. The drilling, which is still in progress, is financed by the Department of Scientific and Industrial Research, and forms part of a programme of geological and geophysical investigation by the Durham Colleges Geology Department.

The background of the operation is as follows. The lead–zinc–fluorine–barium deposits, which occur as veins and replacements in the Carboniferous rocks of the northern Pennines, were shown by K. C. Dunham[1,2] to exhibit a concentric pattern of regional mineral zones, suggesting that mineralization was due to heated solutions, rising at a limited number of centres, and thereafter distributed laterally along channels conditioned by hard beds in the Yoredale sequence. Acid magmatic activity at depth was considered to be a possible source of the solutions. Later on, M. H. P. Bott and D. Masson-Smith[3], following up a strong negative Bouguer anomaly, first noticed during a traverse by J. Hospers and P. L. Willmore[4], made a detailed gravimeter survey of the region. This revealed a negative gravity anomaly of 35 milligals amplitude closely similar in character to the gravity field over exposed granitic batholiths with roof cupolas, such as the Cornubian batholith. Furthermore, certain features of the anomaly were considered to be inconsistent with interpretation as a sedimentary basin. Under the Alston Block, the cupolas indicated by the gravity survey correspond exactly with the postulated emanative centres of the mineralization. When the gravity survey was published, it was suggested that the most probable explanation was that a granite of Permo-Carboniferous age underlay the area, and that it not only supplied the mineralization, but also contributed to the devolatilization of the coal seams in the area. Using a method of calculation devised in collaboration with R. A. Smith, Bott[5] showed from the magnitude of the second derivative of the anomaly that the top surface could not be deeper than 3,500 ft. below Weardale. No upper limit to the depth can be placed from the gravity data, but having regard to the fact that no contact metamorphism is seen in the exposed Carboniferous rocks except near the Whin Sill, he concluded that the probable depth was between 2,000 and 3,000 ft. The postulated granite has become known as the 'Weardale granite'.

The borehole commenced near the top of the Great Limestone, 350 ft. from the surface position of the hanging wall of the Red Vein, one of the most

powerful W.N.W. channels of mineralization in the district, with a yield so far of 460,000 tons of fluorspar and 48,000 tons of galena. The collar of the boring is also 500 ft. from the hanging wall of the E.N.E. Boltsburn Vein, a weak but very persistent fracture, which has yielded 143,000 tons of galena, mainly from associated replacements. Both veins dip towards the boring, which was sited so as to pass through them at depth. Below the Great Limestone, the base of which is taken as the Viséan–Namurian boundary in northern England, a normal Middle Limestone Group succession was encountered. Two quartz-dolerite sills were proved in these beds; the Little Whin Sill, 6 ft. thick, is intruded into the Three Yard Limestone, and the Great Whin Sill, 200 ft. thick, lies beneath the Jew Limestone. The base of the Middle Limestone Group remains to be defined exactly when the faunal study of the cores has been carried out, but the expected change from dark blue-grey limestone to pale grey limestone shows the approximate position of this boundary. The Lower Limestone Group is represented by an alternation of light grey limestones, shales and sandstones; no massive Melmerby Scar Limestone such as is present below Cross Fell is developed; but the typical 'pseudo-breccia' lithology characteristic of this limestone is present in some of the bands. Beneath these light-coloured limestones, black shale with very thin quartz- and feldspar-bearing conglomerate beds rest directly on weathered granite which in a few feet gives place to fresh, well-foliated microcline-quartz-muscovite-oligoclase rock. The foliation is nearly horizontal, and aplite and pegmatite bands occur at various angles.

So far, ten intersections of metalliferous mineralization have been made. Of eight in the Carboniferous, three are horizontal replacements in limestone and one of these is 16 ft. thick, rich in green fluorite and sphalerite. Two typical Pennine Zone I veins, carrying pyrrhotite, fluorite, quartz, have been intersected within the granite at 1,349–1,363 ft. and at 1,585–1,656 ft., the latter being accompanied by extreme alteration of the granite.

Two definite conclusions may be drawn at this stage: (1) the granite so far proved is of pre-Carboniferous age; (2) the mineral veins were fed from some source beneath that part of the granite so far drilled. To these may be added the suggestion that the buried pre-Carboniferous cupolas served to localize the upward flow of mineralizing fluids into the Carboniferous rocks.

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[1] Dunham, K. C., *Quart. J. Geol. Soc.*, **90**, 689 (1934).
[2] Dunham, K. C., "Geology of the Northern Pennine Prefield", *Mem. Geol. Survey* (1948).
[3] Bott, M. H. P., and Masson-Smith, D., *Geol. Mag.*, **90**, 127 (1953); *Quart. J. Geol. Soc.*, **113**, 93 (1957).
[4] Hospers, J., and Willmore, P. L., *Geol. Mag.*, **90**, 117 (1953).
[5] Bott, M. P. H., *Geol. Mag.*, **97**, 511 (1960).

Isotopic Ages of the Weardale Granite

Age determinations have been carried out on muscovite from the Weardale Granite[1] by both the rubidium–strontium and potassium–argon methods. One specimen from a depth of 1,396 ft. in the borehole was measured by both methods, while another from 1,314 ft. was measured by the potassium–argon method only.

Isotopic dilution techniques were employed for the determination of rubidium, strontium and argon. A flame photometric method was employed to determine potassium. The results for the rubidium–strontium method are given in Table 1, and those for the potassium–argon method in Table 2.

Table 1. Rubidium–Strontium Determinations on Muscovite

Depth of sample (ft.)	Rubidium (p.p.m.)	Normal strontium (p.p.m.)	Radiogenic strontium (p.p.m.)	Age (m.yr.)
1,396	767	19·4	1·15	360 ± 12
1,396	757	19·6	1·15	365 ± 12

Decay constant of rubidium-87 = $0{\cdot}1475 \times 10^{-10}$ yr.$^{-1}$

Table 2. Potassium–Argon Determinations on Muscovite

Depth of sample (ft.)	K_2O (per cent)*	Weight fused (gm.)	Radiogenic argon (p.p.m.)	Atmospheric argon (per cent)	Age (m.yr.)
1,396	10·01	2·034	0·240	17·4	370 ± 10
1,314	10·26	3·291	0·239	24	356 ± 12

Decay constants of potassium-40: $\lambda_\beta = 0{\cdot}584 \times 10^{-10}$ yr.$^{-1}$
$\lambda\beta = 4{\cdot}72 \times 10^{-10}$ yr.$^{-1}$
Isotopic abundance of potassium-40 = 0·0119 atom per cent
* Potassium analyses by Dr. N. J. Snelling.

All the results agree within the limits of error. Agreement between the two methods makes it highly probable that the weighted mean of the four figures is close to the true age of emplacement of the granite.

The following points may be noted: (i) The weighted mean of 362 ± 6 million years corresponds to a Middle or Late Devonian age of emplacement, according to the latest time-scales[2,3]. The isotopic results therefore agree with the borehole evidence for the pre-Carboniferous age of the granite. (ii) The age of the Northern Pennine mineralization from the field evidence[4] is undoubtedly post-Carboniferous and probably pre-Tertiary. From lead isotope measurements by Moorbath[5] the mean model age of Northern Pennine galenas is 280 ± 30 million years, indicating that the mineralization is in fact of Hercynian age. Thus, from the lead isotope data and the absolute ages, as well as from the observations reported in the preceding communication, the northern Pennine mineralization is not connected with the emplacement of the Weardale granite. (iii) The weighted mean of 362 ± 6 million years for the Weardale granite is significantly younger than the dates for the Shap granite given by Kulp *et al.*[6]. These authors obtained 391 ± 7 million years by the potassium–argon method and 381 ± 7 million years by the rubidium–strontium method. Unpublished rubidium–strontium results obtained at Oxford on the Skiddaw granite suggest that the latter may be contemporaneous with the Weardale granite.

We are indebted to Prof. Dunham for supplying the material for this investigation.

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[1] Dunham, K. C., Bott, M. H. P., Johnson, G. A. L., and Hodge, B. L. (preceding communication).
[2] Holmes, A., *Trans. Edin. Geol. Soc.*, **17**, 183 (1960).
[3] Kulp, J. L., *Rep. Twenty-first Session Internat. Geol. Congress*, Part III, 18 (1960).
[4] Dunham, K. C., *Trans. Geol. Soc. Glasgow*, **21**, Part III, 396 (1952).
[5] Moorbath, S., *Nature*, **183**, 595 (1959).
[6] Kulp, J. L., Long, L. E., Giffin, C. E., Mills, A. A., Lambert, R. St. J., Giletti, B. J., and Webster, R. K., *Nature*, **185**, 495 (1960).

CRYSTALLOGRAPHY

Highly Oriented Boron Nitride

Pyrolytic graphite deposited on a hot target[1] has been found to have a structure with highly oriented crystallites[2]. We have now prepared, similarly, by vapour phase pyrolysis and deposition on a hot target, a boron nitride the structure of which also has a high degree of orientation of its crystallites. Utilizing boron-bearing gases and regulating the parameters of the treatment, we have been able to control the deposit of the pyrolytic boron nitride.

The X-ray diffraction pattern of pyrolytic boron nitride, Fig. 1, shows the structure to be composed of crystallites which are highly oriented with respect to each other and essentially parallel to the deposition surface. The stacking of the basal planes within the crystallites is considered to be turbostratic as indicated by the expanded unit cell height. On the other hand, the diffraction pattern of normal boron nitride reflects the random orientation of the crystallites, but within these the basal planes are well ordered. The diffraction patterns are compared in Fig. 1 with the powdered sample scan intensity having twice the scale factor of the pyrolytic. The trace of the pyrolytic material has been amplified to enhance the low-intensity peaks.

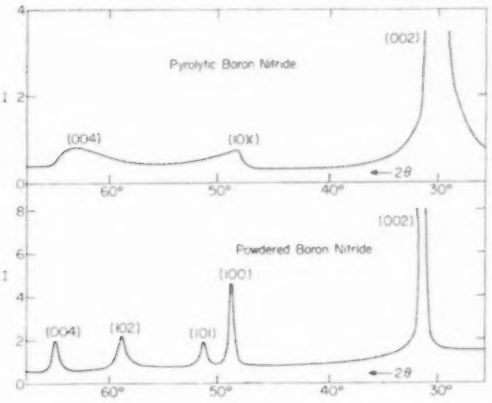

Fig. 1

Boron nitride has a simple hexagonal lattice with unit cell dimensions of $a = 2{\cdot}50399 \pm 0{\cdot}00005$ Å. and $c = 6{\cdot}6612 \pm 0{\cdot}0005$ Å. (ref. 3). The height of the unit cell of the pyrolytic material has been measured as 6·72 Å. using iron-filtered cobalt $K\alpha$ radiation on a General Electric *XRD*-5 diffractometer. Our experience indicates that the a-dimension of the unit cell, the chord of the hexagonal net in the basal plane, is not significantly different in pyrolytic graphite from natural graphite. Therefore, we do not expect any significant change in the edge-length of the pyrolytic boron nitride compared with the published data; this value has been assumed for calculation. The measurement of the edge-length of the pyrolytic unit cell is planned. Crystallite size has been determined to be approximately 140 Å. The theoretical density of normal boron nitride is reported[3] as 2·27 gm./c.c., compared with 2·26 gm./c.c. for pyrolytic boron nitride calculated with the above data.

Spectrochemical analysis of the pyrolytic material shows a relatively pure material with only trace concentrations of impurities. Observed impurities are magnesium, molybdenum and silicon at levels of about 10 parts per million or less.

The material is deposited on the hot target as a dense, fine-grained piece. Thin pieces are transparent and fairly thick (1/2 mm.) pieces are translucent. Samples have been obtained with either white or yellow colouring. Specimens of the white and yellow material have been examined by X-ray and chemical analysis and by neither method can we discriminate between the colours. Microstructure of the material shows the columnar cones characteristic of those found in the vapour deposition of the pyrolytic graphite. Fig. 2 is a photomicrograph of a representative section, the surface of the initial deposit being at the apex of the growth cones. Examination of the optical characteristics has been initiated, but results are not available for this preliminary report.

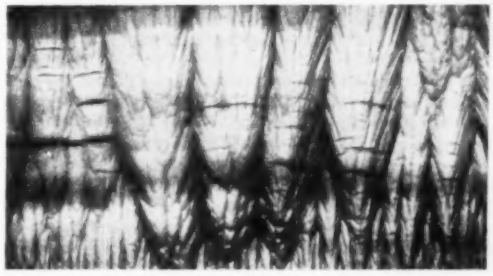

Fig. 2

These are the initial results from the investigation of pyrolytic boron nitride. The work reported is one phase of a broader programme to gain better understanding of the single crystal properties of selected refractory materials such as graphite, graphitic alloys, carbides, nitrides and related compounds for which adequate single crystals are not available. The technique of pyrolytic preparation produces samples with highly oriented structures that can be used in place of single crystals for investigation of some properties of the materials. Thus, the preparation of the highly oriented boron nitride is an approach to, and will permit the examination of, single-crystal characteristics of boron nitride so that the effect of its lattice anisotropy can now be investigated. It is expected that the wide interlayer spacing compared with the interatomic distance within the plane will generate significant anisotropy of the fundamental physical properties of boron nitride.

We thank R. Mozzi for his assistance and co-operation in obtaining diffraction data.

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[1] Brown, A. R. G., Hall, A. R., and Watt, W., *Nature*, **172**, 1145 (1953).
[2] Guentert, O. J., and Prewitt, C. T., *Bull. A.P.S.*, II, **5**, 187 (1960).
[3] Pease, R. S., *Acta Cryst.*, **5**, 356 (1952).

PHYSICS

Rates of Recombination in Hydrogenic Plasmas

In common with other experimental determinations of rates of recombination of ions with electrons[1], recent spectroscopic observations of the afterglow of the *Zeta* discharge have indicated that these rates are much greater than simple theory predicts. When comparison has been made with the theory of radiative recombination[2–4], including recombination into all the excited levels of the atom, the theoretical value falls short of the experimental. Another primary process is three-body recombination. This is the inverse of ionization by electron collision to which it is related by the principle of detailed balance in thermodynamic equilibrium. The theory of collisional ionization was developed classically by Thomson[5], and if three-body recombination-rates into the ground-state are computed from this theory they also are found to be quite inadequate to explain the experimental observations.

In this communication there is proposed a more complex recombination mechanism which is based on well-known atomic collision processes, and which may help to explain the observed values. The three-body recombination-rate (derived from the classical ionization-rate) is proportional to the fourth power of the principal quantum number of the state into which the electron falls. Thus there is the possibility of three-body recombination into an excited state followed by spontaneous radiative decay being an effective recombination mechanism. This possibility is the kernel of the physical problem investigated here.

Specifically computations have been made of the rate at which the ground-states of hydrogen atoms and of hydrogen-like boron ions (B V, $Z = 5$) are populated as a result of the following processes among the first 20 quantum states of the atom (or B V), the continuum of free electrons and the corresponding bare nuclei: (1) collisional ionization; (2) three-body recombination; (3) collisional transitions between bound states; (4) radiative recombination; (5) spontaneous radiative transitions. The plasma was assumed to be optically thin.

The total rate at which the ground-state is populated is the sum of: (1) direct three-body recombination; (2) direct radiative recombination; (3) collisional transitions from all the excited states; (4) spontaneous decay from all the excited states.

This rate therefore depends on the instantaneous populations of all the excited states. Thus the solution was required of the following set of equations:

$$\frac{dn_{a,i}}{dt} = (\text{rate of populating state } i) - (\text{rate of depopulating state } i)$$

where $n_{a,i}$ is the population of the state having main quantum number i. Low-energy collisions are assumed to be sufficiently frequent to ensure that the substates are populated relatively according to their statistical weights. These equations were solved using the steady-state approximation $\left(\frac{dn_{a,i}}{dt} = 0, i \neq 1\right)$.

This is legitimate for hydrogen atoms and hydrogen-like ions because transitions among the excited states and the continuum are much more probable than transitions to and from the ground-state. Excluded from the computed rate of populating the ground-state are processes where the ground-state electron is raised to an excited state by collision and then returns to the ground-state by either a radiative or collisional transition.

In deciding the uppermost quantum state to be taken into account I noted the equivalence of situations (*a*) where states have a Saha distribution of populations and (*b*) where there is an imaginary continuum of electrons having a Maxwellian distribution of velocities, extending over the same energy region, and being suitably quantized. Thus, in making the discrete states merge into the imaginary continuum at the twentieth state, it was necessary to check in each case considered that at least the states immediately below twenty were Saha-populated. This was shown to be so for the range of conditions considered.

Cross-sections, due to M. J. Seaton (private communication), and *f*-values calculated by Green *et al.*[6], were used. Seaton derived his expression specifically for ions, but its similarity to the classical Thomson expression justifies its use for atoms. The calculations were done on a *Mercury* (Ferranti) electronic computer.

The results are presented in Fig. 1 in terms of a correction factor which is the amount by which the ground-state radiative recombination-rate has to be multiplied to give my computed-rate of populating the ground-state.

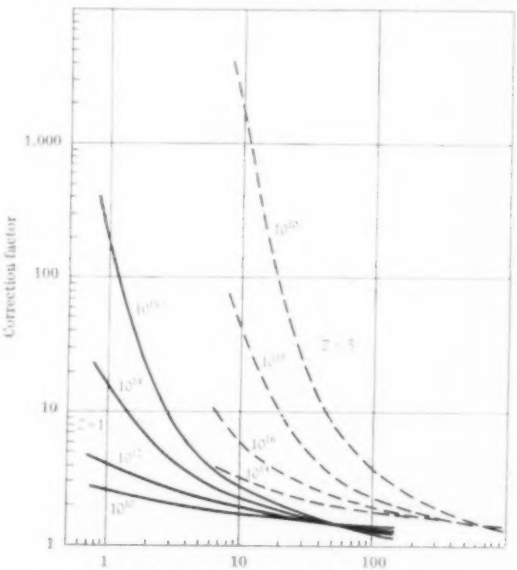

Fig. 1. Computed rates of populating the ground-states. The curves are for ions having nuclear charges 1 and 5 and for various electron densities (cm.$^{-3}$)

$$\text{Correction factor} = \frac{\text{Computed rate of populating the ground-state}}{\text{Radiative recombination-rate into the ground-state}}$$

The departures of the populations of the states from their Saha values is illustrated in Fig. 2 ($kT_e = 1$ eV.). In this connexion it is useful to designate a particular state which approximately marks the lower limit of the Saha region of the term scheme as the 'collision limit'. I define it as the lowest state for which the bound electron has a greater probability of making a transition to an upper state than to a lower state. The collision limits are marked on Fig. 2. The broken curve of this diagram depicts

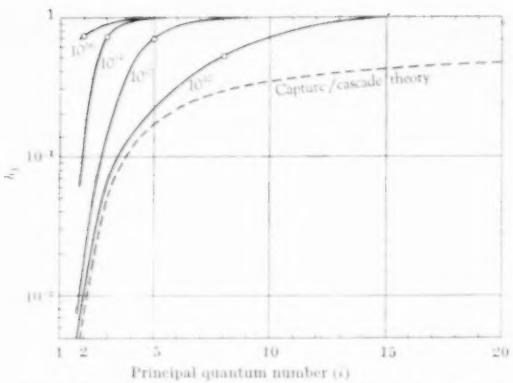

Fig. 2. Populations of the excited states of hydrogen in a recombining plasma at an electron temperature $kT_e = 1$ eV. The curves are for various electron densities (cm.$^{-3}$)

$$b_i = \frac{\text{Calculated population of state } i}{\text{Saha population of state } i}$$

Collision limits.

the case where radiative processes only are taken into account. This case was worked out by Seaton[7].

The set of curves of Fig. 2 illustrates clearly the effect of increasing density on the mechanism by which electrons leave the continuum and become bound. In the limit of very low density, radiative recombination is the only mechanism, and the states are populated according to the capture-cascade theory. However, the curves of Fig. 1 do not tend to unity because radiative recombination into upper states followed by spontaneous decay make a contribution. Such processes are more important at low density and this explains the cross-over of the curves of Fig. 1. As the density increases, the upper states progressively become populated more closely according to the Saha distribution. This is due to the increasing influence of collision processes (including three-body recombination).

The computed values for the rate of populating the ground-state may be compared with the experimentally observed ion decay-rates for the hydrogen plasma of *Zeta*[8]. For the conditions of the measurement the plasma parameters were (to a factor 2) $n_e = 10^{13}$ cm.$^{-3}$, $kT_e = 1$ eV. The rate at which the ion population decayed was about ten times greater than the radiative recombination-rate, in agreement with my computed value.

Since the work reported here was done, there have appeared two reports on similar calculations[9,10]. The results of Bates and Kingston are in good agreement (±30 per cent) with mine. Besides providing useful confirmation of this other work, I have investigated the effect of ionic charge, have extended the calculations to higher-electron temperature, and have presented the computed populations of the excited states.

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[1] Loeb, L. B., *Handbuch der Physik* (Berlin), **21**, 471 (1956).
[2] Kramers, H. A., *Phil. Mag.*, **46**, 836 (1923).
[3] Milne, E. A., *Phil. Mag.*, **47**, 209 (1924).
[4] Gaunt, J. A., *Phil. Trans. Roy. Soc.*, A, **229**, 163 (1930).
[5] Thomson, J. J., *Phil. Mag.*, **23**, 449 (1912).
[6] Green, L. C., Rush, P. P., and Chandler, C. D., *Astrophys. J.* (Supp. 26), **3**, 37 (1959).
[7] Seaton, M. J., *Mon. Not. Roy. Astro. Soc.*, **119**, 90 (1959).
[8] McWhirter *et al.* (in the press).
[9] D'Angelo, N., *Phys. Rev.*, **121**, 505 (1961).
[10] Bates, D. R., and Kingston, A. E., *Nature*, **189**, 652 (1961).

Doubling of the Proton Magnetic Resonances of Certain Organophosphorus Compounds

We have found that some of the proton magnetic resonances of the alkyl groups of several types of organophosphorus compounds are doubled. This doubling is in addition to the resonance multiplication that would be predicted from coupling with other magnetic nuclei in these compounds. So far we have observed resonance doubling for three types of structures. Type (I) is exemplified by 2-propyl phenylphosphinyl chloride. In compounds of this type, the alkyl group is directly linked to the phosphorus atom. Type (II) is exemplified by di-2-butyl phenylphosphate or di-2-butyl phenylphosphonate. In such compounds the alkyl group is linked through an oxygen atom to the phosphorus atom. Type (III) is exemplified by di-2-propyl phenylphosphonite, in which the phosphorus is trivalent.

It seems probable that the resonance doubling with type (I) compounds is due to the same sort of hindered rotation that produces resonance multiplication in substituted ethanes[1,2]. However, in the case of type (I) compounds the axis of rotation is the bond between the α carbon atom and the phosphorus atom rather than between two carbon atoms. A Fisher–Hirschfelder–Taylor model of the 2-propyl phenylphosphinyl chloride shows that if one of the rotational isomers is energetically preferred over the other two, then, on the average, one of the methyl groups is closer to the benzene ring than is the other. Since the benzene ring possesses a relatively strong induced magnetic field, the methyl groups would, on the average, be in different magnetic environments, and two sets of resonance signals would result.

We have, at present, only an incomplete concept of the structural features that cause resonance doubling in type (II) compounds. It seems likely that the same structural effects that cause doubling in type (I) also cause the resonance doubling for type (II). However, the situation is complicated by the intervention of an oxygen atom between the phosphorus atom and the α carbon atom of the alkyl group. The resonance doubling in type (II) compounds was observed only when the molecule contained one aromatic substituent and when the alkyl group was linked through an internal carbon atom. Di-1-alkyl phenylphosphates and di-1-alkyl phenylphosphonates did not exhibit the doubling. Qualitative proton

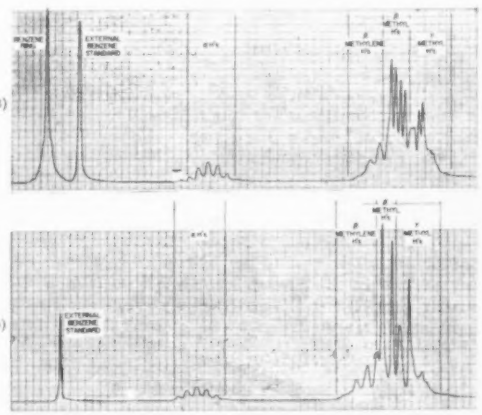

Fig. 1. (*a*) Di-2-butyl phenylphosphate. (*b*) Tri-2-butyl phosphate

resonance spectra of (*a*) di-2-butyl phenylphosphate and of (*b*) tri-2-butyl phosphate are given in Fig. 1. These spectra were run at 40 Mc./s. on a Varian nuclear magnetic resonance spectrometer, model *V-4300B*.

There is no background of experience with this type of resonance doubling in structures similar to that of type (III). However, it is perfectly evident that there must be conformations of type (III) that represent lower potential energies than other conformations. If in these conformations the two methyl groups in a 2-propyl radical are not interchanged with respect to their proximity to the benzene ring, then resonance doubling can occur. This is true since the average magnetic environment of the protons of the two methyl groups would be different.

We are continuing our investigations of the proton magnetic resonances of these three types and related compounds.

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[1] Drysdale, J. J., and Phillips, W. D., *J. Amer. Chem. Soc.*, **79**, 319 (1957).
[2] Nair, P. M., and Roberts, J. D., *J. Amer. Chem. Soc.*, **79**, 4565 (1957).

RADIATION CHEMISTRY

Photoemission into Liquid *n*-Hexane

Recent measurements of conduction[1] and of ion transit time[2,3] in liquid *n*-hexane have made use of the fact that electrons can be released into the liquid by the incidence of ultra-violet illuminations on the cathode surface. These measurements have been interpreted with the assumption that the ultra-violet light can be passed through the liquid to the cathode surface without producing ions in the liquid or otherwise disturbing it. Even in the most highly purified *n*-hexane it is not certain that this is true, particularly when subject to electric stress. The method described here attempts to overcome this difficulty.

Ultra-violet light is directed through a quartz window, attached to the liquid cell, on the inside of which is deposited a thin metal film cathode. Electrons are ejected from the opposite surface of the film into the liquid. By depositing a film of suitable thickness it is possible to produce a reasonable emission current without appreciably irradiating the liquid. Other advantages are that the area of the cathode illuminated can be controlled accurately and localized within the uniform field region, an important factor if current saturation is to be examined; and the spacing between electrodes in the cell can be made very small if desired, since the need for a large spacing for oblique illumination is removed. This will allow much higher fields to be attained with reasonable voltages.

The test cell was constructed from a short length of 2-in. diameter glass tubing, with a ground-glass flange at one end to hold the anode assembly. The opposite end was carefully ground to ensure that the electrodes were parallel. Both electrodes were sealed to the cell with cold-setting 'Araldite' since it was found that neoprene 'O' rings contaminated the liquid. The anode was a stainless steel disk, 1 in. in diameter; and in the present experiments the cathode film was aluminium with a transmission for visible light of about 50 per cent. The spacing between the electrodes was $3{\cdot}74 \times 10^{-2}$ cm., and they were parallel to within $\pm$ 2 per cent over the uniform field region. Finally, the cell was incorporated into a simple distillation system which allowed the liquid to be degassed at a pressure of about 10^{-3} mm. mercury.

After 24 hr. at a stress of 10 kV./cm., the residual conductivity of the liquid was less than 10^{-16} mho./cm., and on irradiating the outside of the cathode with ultra-violet light the current increased initially by a factor of 10^3. However, this did not remain constant but decreased slowly over a period of 20 min. by a factor of about 3. On switching off the ultra-violet illumination, slow-time effects were also observed in the decrease of conductivity. Morant[1] found similar slow variations for the case of direct illumination of the cathode through the liquid.

By reversing the polarity it was found that the current injected into the liquid with the metal film as cathode was about 100 times that injected with the film as anode. The fact that there was a current when the film was positive indicated that some radiation was passing through the film and either releasing electrons from the stainless steel electrode or photoionizing the liquid. The ratio of the two currents remained the same when the cell was emptied and evacuated, and this suggests that the currents originated at the electrodes and not in the bulk of the liquid. More careful control of the film thickness should allow the amount of radiation passing into the liquid to be reduced.

With the cell evacuated the current from the film became saturated with increasing voltage, and was about 10^{-8} amp. In the liquid for the same field and illumination intensity the current was approximately 10^{-11} amp. The variation of photocurrent with increasing field up to 700 V./cm. in *n*-hexane has been reported by Morant[1], and with the present experimental arrangement a similar variation was observed over the same field-range (curve *a*, Fig. 1). At higher fields,

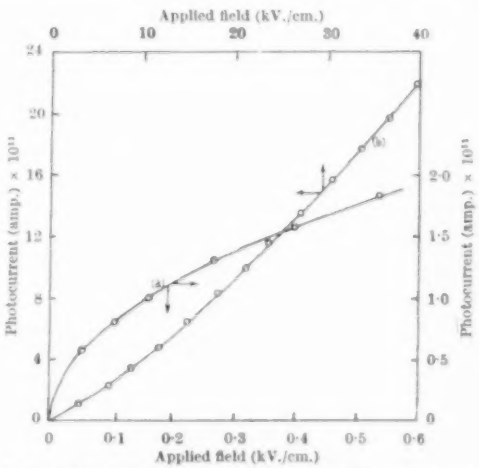

Fig. 1. Photocurrent injected into *n*-hexane for various field strengths with constant ultra-violet illumination

however, there is a marked change, and the current increases with increasing field (curve *b*, Fig. 1). Above 10 kV./cm. the current varies with field as $E^{1.21}$.

Although the equipment used was not designed for mobility measurements, an estimate of the mobility of the negative ion in *n*-hexane can be made from the transient growth of current immediately after switching on the ultra-violet light, and the value so obtained (about 8×10^{-4} cm.^{2} V. sec.) is in rough agreement with other published data[2,3].

The experiments described here show that it is possible to inject an appreciable current into a dielectric liquid without having to subject the liquid to intense radiation. The fact that the current can be confined to the centre of the uniform field region is of great importance in the study of transient phenomena in which electrode edge effects can give rise to appreciable error. Also, the long time decay of current which is observed after the ultra-violet light is switched on would not be important if pulsed illumination were used, and the amount of charge injected into the liquid during the pulse would be considerably greater than that calculated from the magnitude of the steady current.

This work is part of a programme which is receiving financial support from the Department of Scientific and Industrial Research. I wish to thank Prof. M. W. Humphrey Davies for facilities provided, and Dr. T. J. Lewis for his encouragement and helpful discussions.

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[1] Morant, M. J., *Nature*, **187**, 48 (1960).
[2] LeBlanc, O. H., *J. Chem. Phys.*, **30**, 1443 (1959).
[3] Chong, P., and Inuishi, Y., *Tech. Rep. Osaka Univ.*, **10**, 545 (1960).

The Importance of Hydroxyl Radicals as Intermediates in the Cross-linking of High Polymers by γ-Irradiation

We have irradiated thin gelatin films (thickness 0·5–1·0 mm.) with cobalt-60 γ-rays at a dose-rate of $4{\cdot}2 \times 10^4$ r. hr.$^{-1}$ at 10° C. The film was either suspended in a stoppered bottle containing oxygen or nitrogen or immersed in a liquid which filled the bottle. After irradiation of the film, attempts were made to dissolve it in 19 times its own weight of water at 40° C., and the viscosity of any resultant solution was measured. No increase in relative viscosity was observed when the irradiation was carried out in an atmosphere of oxygen or nitrogen, or when the film was suspended in liquid paraffin, benzene, ether, *cyclo*hexanone, pyridine, acetone or an alcohol, even when the dose exceeded 1 mega-roentgen. In the presence of water, however, the gelatin became cross-linked, as was shown by the fact that it was merely swollen by treatment with boiling water.

In a second series of experiments, gels prepared by dissolving 50 gm. of gelatin in 1 litre of water at 40° C. followed by 1 hr. in an ice-bath were irradiated at 10° C. immediately after covering with a layer of an organic liquid. Liquids such as methanol, glycerol and ether markedly reduced the cross-linking in that part of the gel which they had penetrated. These experiments indicate that cross-linking of gelatin induced by radiation is dependent on generation of free radicals by the action of the γ-rays on water, and that these radicals attack gelatine in reactions which probably involve abstraction of hydrogen atoms, thereby forming free radicals on the gelatin chains which become the cross-linking sites. Any organic liquid present diminishes the cross-linking either by competing with the gelatin for radicals from the water or by interfering with the cross-linking process.

If, as our results suggest, radicals play an important part in radiation-induced cross-linking of polymers, the otherwise anomalous results of Okada, Ito and Amemiya[1] may readily be explained. These authors observed that an atmosphere of nitrous oxide promotes the cross-linking of polyethylene induced by γ-irradiation, whereas an atmosphere of oxygen retards it. Dainton *et al.*[2] have shown that nitrous oxide reacts rapidly with hydrogen atoms (reaction 1) with formation of hydroxyl radicals and nitrogen.

$$H\cdot + N_2O \rightarrow HO\cdot + N_2 \qquad (1)$$

and it is known that oxygen 'scavenges' hydrogen atoms to form $HO_2\cdot$ radicals which are likely to be less effective than $HO\cdot$ radicals in causing cross-linking.

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[1] Okada, Ito and Amemiya, *Third Conf. Radiation Chemistry, Tokyo, October 16, 1960*).
[2] Dainton, Peterson and Sills, *Nature*, **186**, 878 (1960).

CHEMISTRY

Prediction of Retention Data in Gas–Liquid Chromatography from Molecular Formulæ

As a result of the introduction of the R_{x9} method[1,2] of presenting gas–liquid chromatographic retention ratios, it has been possible to derive a simple method of predicting retention data from a knowledge of molecular weight and structure. Preliminary investigations have indicated its value in the structural analysis of organic compounds.

The retention index (I) of Kovats[4] is closely related to R_{x9} by the following expression (ref. 2):

$$I' = \frac{\log R_{x9}}{b} + 9$$

where I' is $I/100$ and b the slope of the log plot for *n*-paraffins. I' can be interpreted as the carbon number of a hypothetical *n*-paraffin having the same retention as the solute to which I' refers. The formula of the hypothetical *n*-paraffin equivalent to the solute is $C_I{\cdot}H_{2I'+2}$ and will have a molecular weight given by $M_e = 14{\cdot}026\,I' + 2{\cdot}016 = 14{\cdot}026\,\frac{\log R_{x9}}{b} + 128{\cdot}25$. This can be regarded as the 'effective' molecular weight of the solute. We have found the difference between the effective and true molecular weights of the solute (ΔM_e) to be a useful parameter for correlating retention data with chemical structure for the following reasons:

(1) ΔM_e is a conceptually simple parameter having the familiar dimensions of molecular weight.

(2) It is virtually constant throughout a homologous series (Table 1).

(3) It has no, or only a slight linear, variation with temperature (Table 2).

(4) ΔM_e is an additive function of the structural features of a molecule (Table 3) (except when specific group–group interactions occur).

Table 1. ΔM_e values of homologous series (65° C.)

Compound or class	Stationary phase	R_{Ex}	b	ΔM_e
Acetone	DNP	0·069	0·377	+27·0
Methyl ethyl ketone	DNP	0·163	0·377	+26·7
Methyl n-propyl ketone	DNP	0·345	0·377	+24·9
Methyl n-butyl ketone	DNP	0·841	0·377	+25·3
Butan-1-thiol	Squalane	0·152	0·391	+8·7
Pentan-1-thiol	Squalane	0·381	0·391	+8·7
Hexan-1-thiol	Squalane	0·939	0·391	+9·0
Heptan-1-thiol	Squalane	2·323	0·391	+9·1
Oct-1-ene	PEG 400	0·740	0·301	+9·1
Dec-1-ene	PEG 400	2·725	0·301	+9·3
Dodec-1-ene	PEG 400	10·02	0·301	+8·9
n-Alkane thiols	DNP	—	0·377	+20·0*
	Squalane	—	0·391	+8·9*
	PEG	—	0·301	+49·4*
n-Alcohols	DNP	—	0·377	+40·0*
	PEG	—	0·301	+106·7*
Alk-1-enes	DNP	—	0·377	+1·6*
n-Alkane bromides	DNP	—	0·377	−24·2*
n-Alkane cyanides	DNP	—	0·377	+45·8*
n-Alkane acetates	DNP	—	0·377	+8·3*

* Mean value for at least 4 homologues.

Table 2. Variation of ΔM_e with Temperature

Compound	On 20 per cent di-nonyl phthalate/'Celite'		
	20° C.	65° C.	100° C.
t-Butanol	+21·7	+18·5	+16·0
Di-t-Butyl peroxide	−39·7	−40·6	−41·5
Butan-1-thiol	+19·2	+19·7	+20·1
Oct-1-ene	+1·9	+2·3	+2·1

The column b factors were 20°, 0·477; 65°, 0·377; 100°, 0·311.

Table 3. Effective Molecular Weights of α,ω Dithiols on Squalane at 65° C.

Compound	Calculated* M_e	Calculated* R_{Ex}	Found R_{Ex}	Found M_e
Ethane-1 : 2-dithiol	111·9	0·350	0·320	110·5
Propan-1 : 3-dithiol	126·0	0·866	0·838	125·5
Butan-1 : 4-dithiol	140·0	2·268	2·268	140·0

* Using ΔM_e for SH group of 8·88.

(5) For a proposed structure, M can be computed and ΔM_e for the various structural features obtained from correlation tables. Thus M_e and hence R_{Ex} can be predicted. This has proved invaluable in identifying the products of a reaction where only a few alternatives are possible. Thus, once ΔM_e functional group correlation charts are available, retention times can be predicted without any prior chromatography. This is not practicable with the methods at present available.

(6) ΔM_e values of selected functional groups may be used to characterize chromatographic columns, particularly when the retention data are to be published. Thus, it should be possible to use the gas-liquid chromatography data confidently in the literature for the solution of everyday analytical problems.

(7) In general, ΔM_e values need to be expressed to fewer significant figures than I' contributions.

Work on the compilation of ΔM_e values and the application to column characterization, structural analysis and intramolecular interactions is proceeding in these laboratories and will be published in due course.

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[1] Smith, J. F., *Chem. and Indust.*, 1024 (1960).
[2] Evans, M. B., and Smith, J. F., *J. Chromatog.* (in the press).
[3] Smith, J. F., *Proc. Third Gas Chromatography Symp.*, edit. R. P. W. Scott, 270 (Butterworths, London, 1960).
[4] Kovats, E., *Helv. Chim. Acta*, **41**, 1915 (1958).

Trimerization of Nickel-(II) Acetylacetonate in Solution

Following Bullen, Mason and Pauling's confirmation of the trimeric structure of anhydrous nickel-(II) acetylacetonate[1], we report evidence for the persistence of the trimeric structure in solution.

We have prepared the anhydrous compound from the dihydrate both by vacuum sublimation and by azeotropic drying of toluene solutions, the latter method providing a particularly convenient means of obtaining water-free solutions. Cryoscopic molecular weight determinations on solutions of the anhydrous compound in benzene (dried over anhydrous magnesium perchlorate) gave the following results:

Weight of benzene (gm.)	23·12	23·12	23·12
Weight of acetylacetonate (gm.)	0·0985	0·2050	0·3185
Depression of freezing point (° C.)	0·027	0·059	0·093
Molecular weight	819	770	759

the mean molecular weight of 779 comparing well with a theoretical value for the trimer of 771.

Addition of water to solutions of the anhydrous compound in toluene precipitated the dihydrate; addition of ethanol precipitated the corresponding di-ethanolate and of pyridine the di-pyridine adduct, the solubility of which was high enough to permit spectrophotometric examination of the equilibrium:

anhydrous compound + pyridine $\rightleftarrows$ pyridine adducts.

Absorption curves for various ratios of the reacting species passed through one of two distinct isosbestic points, indicating a two-stage addition, but with considerable overlap of the two stages. However, by taking advantage of the variable reactivity of different heterocyclic bases we have been able to examine the two stages independently; thus, 4-methyl-pyridine gave virtually complete conversion to the 1 : 1-adduct and incomplete conversion to the 1 : 2-adduct, whereas 2 : 6-dimethyl-pyridine gave incomplete conversion to the 1 : 1-adduct without detectable formation of the 1 : 2-adduct. The form of the equilibrium constants for the two stages:

$$k_1 = \frac{[\mathrm{Ni(acac)_2.base}]^3}{[\{\mathrm{Ni(acac)_2}\}_3]\times[\mathrm{base}]^3};$$

$$k_2 = \frac{[\mathrm{Ni(acac)_2.base_2}]}{[\mathrm{Ni(acac)_2.base}]\times[\mathrm{base}]}$$

correspond to the reactions:

$$\{\mathrm{Ni(acac)_2}\}_3 + 3\,\mathrm{base} \rightleftarrows 3\,\mathrm{Ni(acac)_2.base}$$

$$\mathrm{Ni(acac)_2.base} + \mathrm{base} \rightleftarrows \mathrm{Ni(acac)_2.base_2}.$$

The constancy of the equilibrium constants obtained over a wide range of completion of each reaction is shown in Tables 1 and 2.

Bullen, Mason and Pauling's crystal structure determination shows that each nickel atom in the anhydrous trimer is octahedrally co-ordinated by six oxygen atoms, trimerization presumably occurring so as to maintain the co-ordination number of the nickel atoms. It is rather surprising therefore that the intermediate 1 : 1-adducts appear to be monomeric where we might expect dimerization to occur. Recent X-ray analyses of zinc acetylacetonate monohydrate[2] and a triarsine nickel bromide complex[3], however, suggest that five co-ordination may be more common than is often supposed.

Our observation that the trimeric structure, and hence the octahedral co-ordination of the nickel

Table 1. First-stage Equilibrium Constant. Total [Ni] = 25 mgM.-at./L.

[base](mmole/L)	0·0	3·0	6·1	9·3	12·6	16·0	19·5	23·1	26·8	30·5	34·5	∞
Optical density (675 mμ)	0·770	0·750	0·730	0·710	0·685	0·666	0·645	0·635	0·610	0·595	0·585	0·550
Per cent Ni as adduct	0·0	9·1	18·2	27·2	38·6	47·3	57·0	61·5	73·0	80·0	84·0	100
k_1 (mole^{-1})	—	4,800	3,300	3,900	7,200	5,100	5,700	2,550	4,500	3,900	2,700	—

Average k_1 = 4,200 moles^{-1}. Infinity value calculated.

Table 2. Second-stage Equilibrium Constant. Total [Ni] = 25 mgM.-at./L.

[Base](mmole/L)	25·0	30·0	40·0	50·0	65·0	75·0	85·0	95·0	105·0	120·0	∞	
Optical density (575 mμ)	0·320	0·360	0·472	0·520	0·670	0·710	0·755	0·770	0·790	0·830	0·950	
Per cent Ni as adduct	0·0	6·3	24	32	56	62	69	71	75	81	100	
k_2 (mole^{-1})	—	20	35	28	49	47	52	46	49	56	—	

Average k_2 = 42 moles^{-1}. Infinity value calculated.

atoms, is preserved in solutions of anhydrous nickel acetylacetonate clarifies the difficulties which have been met in attempts to interpret the absorption spectra of these solutions. Both Jorgensen[4] and Maki[5] have commented on the similarity between the absorption spectra of the anhydrous and hydrated compounds, interpreting this in terms of ligand-field effects due to axial perturbations by the solvent in solutions of the anhydrous compound or to the smallness of the axial perturbations in the dihydrate. It is now apparent that both substances are examples of nickel-(II) cations in an octahedral environment of six oxygen atoms and the similarity of spectra is to be expected.

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[1] Bullen, G. J., Mason, R., and Pauling, P., *Nature*, **189**, 291 (1961).
[2] Lippert, E. L., and Rutter, M. R., *J. Chem. Soc.*, 4996 (1960).
[3] Mair, G. A., Powell, H. M., and Henn, D. E., *Proc. Chem. Soc.*, 415 (1960).
[4] Jorgensen, C. K., *Acta Chem. Scand.*, **9**, 1362 (1955).
[5] Maki, G., *J. Chem. Phys.*, **29**, 162 (1958).

Mullite Formation in the Aluminium Fluoride–Silica System (AlF_3–SiO_2)

The role of mullite, the conditions and kinetics of its formation are among the main problems of ceramic theory. The equilibrium conditions of the alumina–silica system have been established[1–3]. Grofcsik and Vago[4,5] have given an answer to the problems of kinetics on the basis of results obtained from their investigations carried out on silica gel and alumina. Several authors have dealt with the mineralization of mullite formation too[6–8]. The examination of the AlF_3–SiO_2 system suggests a way which may clear up the problem of possible mullite-formation mechanisms in ceramic products.

The following materials have been used: reagent grade aluminium fluoride with or without structural water, silica gel produced by the hydrolysis of ethyl silane, cristobalite obtained by 1,300° C. heat treatment of the latter, rock crystal and silica glass. All materials were finer than 60μ with similar particle-size distributions. Mixing was done mechanically in an agate mill, the heat treatment in an oxidizing atmosphere.

The gross process may be described by the following equation:

$$12\ AlF_3 + 13\ SiO_2 = 2(3Al_2O_3.2SiO_2) + 9\ SiF_4$$

using materials with structural water[9] by the reaction:

$$AlF_3 + SiO_2.\ xH_2O \rightarrow 3Al_2O_3.2SiO_2 + HF$$

is mentioned, too.

Examinations, however, have been carried out with a slight excess of silica. The samples were measured separately and dried at 105° C.

The reaction kinetics, as a function of heating time and temperature, have been determined by differential thermal analysis and thermogravimetric analysis. The formation of mullite has been detected microscopically and by X-ray diffraction patterns and determined quantitatively by a Muller diffractometer.

The following statements are made:

(1) The formation of silicon fluoride in the AlF_3–SiO_2 system begins at 600 ± 15° C. and is intense at 850–1,000° C.

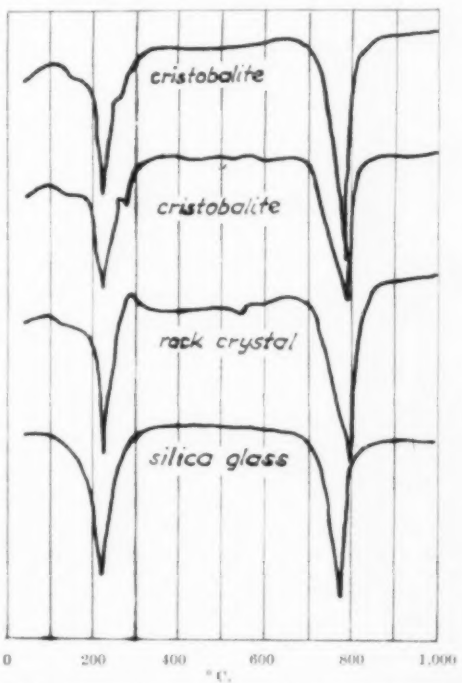

Fig. 1. Differential thermal analysis of various compositions

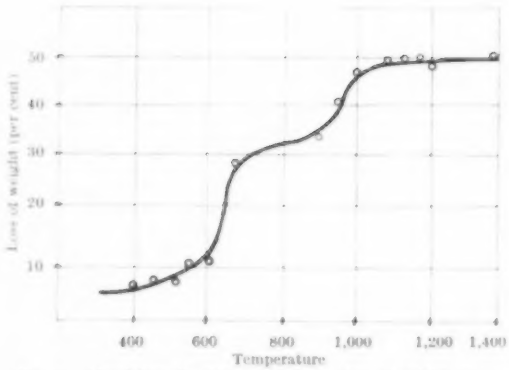

Fig. 2. Aluminium fluoride–cristobalite; loss of weight as a function of temperature

(2) The beginning and development of the reaction is a function of the particle size and the space between particles of the mix.

(3) The beginning of mullite formation does not coincide with the silicon fluoride formation, having a temperature higher by 300–400° C.

(4) The activation energy of mullite formation is lowest in the case of silica glass and higher with all other silica modifications.

(5) The initial temperature of mullite formation is 900 ± 15° C., using a mix of silica glass and aluminium fluoride (particle size less than 60μ) and agglomerated by a pressure of 50 kgm./cm.^{2}.

(6) The quantity of developed silicon fluoride increases at the start exponentially with temperature and is followed by a temporary quasi-steady state. The complete development of silicon fluoride and the simultaneous mullite formation needs further activation energy.

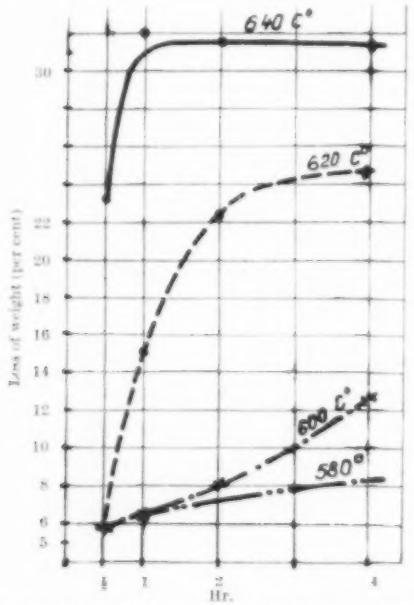

Fig. 3. Aluminium fluoride–cristobalite; loss of weight as a function of temperature and time of thermal treatment

Table 1. X-Ray Diffraction Pattern of the Silica Gel AlF_3 Mixture, Heat Treated 2 hr.

d (kX.)	Intensity	Material	d (kX.)	Intensity	Material
3,718	3	$2Al_2O_3.2AlF_3.3SiO_2$	1,872	3	$2Al_2O_3.2AlF_3.3SiO_2$
3,216	3	,,	1,684	3	,,
3,050	1	,,	1,626	2	,,
2,951	3	,,	1,536	3	,,
2,502	1	,,	1,473	1	,,
2,377	3	,,	1,453	1	,,
2,191	1	,,	1,423	2	,,
2,127	3	,,	1,406	2	,,
2,062	2	,,	1,369	3	,,
1,993	1	,,	1,333	1	,,

Loss of weight against temperature plots, being similar in the case of all silica modifications, are shown in Figs. 2 and 3.

(7) Two endothermal effects are shown by differential thermal analysis in the case of a raw mix made of water containing aluminium fluoride and different silica modifications; the first from 105° to 330° C. and the second from 680° to 850° C. (Fig. 1).

(8) In the case of the aluminium fluoride–silica system the formation of silicon tetrafluoride ensures conditions in which mullite develops more rapidly than in the alumina–silica system. The velocity of mullite formation shows a rapid increase with temperature.

A crystalline and an amorphous fluorine-bearing body is formed at 600 ± 15° C. as proved by X-ray diffraction patterns of materials heat-treated in the interval 600–900° C. (Table 1).

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[1] Bowen, N. L., and Greig, J. W., *J. Amer. Ceram. Soc.*, **7**, 238, 410 (1924).
[2] Toropov, N. A., and Galakhov, F. Ya, *Dok. Akad. Nauk. U.S.S.R.*, **78**, 299 (1951).
[3] Aramaki, S., and Roy, R., *J. Amer. Ceram. Soc.*, **42**, 644 (1958).
[4] Grofcsik, J., and Vágó, E., *Építőanyag*, **4**, 3 (1952).
[5] Grofcsik, J., and Vágó E., *Építőanyag*, **4**, 211 (1952).
[6] Horte, Ch., and Wiegmann, J., *Amer. Ceram. Soc.*, **43**, 9 (1956).
[7] Barta, R., and Barta, Gh., *Zhur. Priklad. Khim.*, **29**, 341 (1956).
[8] Roy, R. *J. Amer. Chem. Soc.*, **39**, 145 (1956).
[9] *Gmelin's Handbuch der anorganischen Chemie*, 151, Sy. Nr. 5; Sy. Nr. 35.

BIOCHEMISTRY

Reactions of Cytochrome-*c* with Methyl Linoleate Hydroperoxide

It is now well known that the oxidation of unsaturated fatty acids and esters is catalysed by a variety of hæmatin protein compounds[1,2]. The effect of cytochrome *c* has been of particular interest to us since we have evidence which conflicts with existing theories regarding the effect of cytochrome *c* on olefinic oxidation.

In our attempts to elucidate the apparent catalytic effect of cytochrome *c*, it was discovered that under certain conditions it could act as an antioxidant, particularly at *p*H's greater than 6·0. With freshly made emulsions of linoleic acid[3] prepared by adding phosphoric acid to a previously heated and then cooled solution of potassium linoleate in a slight excess of alkali, increasing amounts of cytochrome *c* produced longer and longer induction periods, and provided that sufficient cytochrome *c* was added, oxidation could be delayed for hours. Table 1 summarizes the kind of result that has been obtained by measuring the oxygen uptake of 3·3 ml. of an *M*/20 suspension of linoleic acid in *M*/20 phosphate buffer with gelatine as a stabilizer in Warburg manometers at 30°.

Table 1

Concentration of cytochrome *c*	Time (in min.) required for linoleic acid suspension to absorb :						
	0–10 c. mm.	10–50 c. mm.	50–100 c. mm.	100–200 c. mm.	200–300 c. mm.	300–400 c. mm.	400–500 c. mm.
$3{\cdot}50 \times 10^{-5}$ *M*	12	60	7	4½	4	5	5
$3{\cdot}15 \times 10^{-5}$ *M*	9	40	3	4	4½	5	5
$2{\cdot}80 \times 10^{-5}$ *M*	9	33½	5	3½	4½	5½	6½
$2{\cdot}45 \times 10^{-5}$ *M*	3	25	2½	4	5½	6½	9
$2{\cdot}05 \times 10^{-5}$ *M*	2	4	2½	5	6½	8	10½
$1{\cdot}75 \times 10^{-5}$ *M*	2	3	3	6	7½	10	12½

Oxygen uptake in the absence of catalyst is very slow, hours being required for the absorption of the first 10 c. mm. or so. The above results, however, show that cytochrome *c* at high concentrations has an antioxygenic effect in comparison with its behaviour at low concentrations. At $3{\cdot}5 \times 10^{-5}$ *M*, 72 min. are required for the absorption of the first 50 c. mm. and the maximum rate of absorption is reached after about 83 min. At half this concentration of cytochrome, the first 50 c. mm. of oxygen were absorbed in 5 min. and the rate of absorption was at its maximum at this time.

Changes in cytochrome *c* during oxidation experiments have been followed spectroscopically and have shown rapid falls in concentration coinciding with termination of the induction periods.

It seems to us that these phenomena can only be explained by assuming that cytochrome *c* catalyses the breakdown of unsaturated fatty acid peroxides into inactive products, but that during this catalytic process, the cytochrome becomes 'denatured', which is not unusual in enzymatic reactions of this kind, and that the 'denatured' cytochrome has the typical property of catalysing olefinic oxidation. The results that we have obtained depend on the suspensions used being free from traces of peroxides. It has been found, for example, that suspensions prepared by shaking linoleic acid with gelatin solution in an inert atmosphere do not exhibit the above phenomena with those concentrations of cytochrome *c*, and that the amount of heating the potassium soap is subjected to during the preparation of the precipitated suspension has an influence on the length of the induction period produced in the presence of cytochrome. It is thought that trace amounts of peroxide are removed from the linoleic acid in the present instance when the potassium soap is heated in order to bring it into solution.

The effect of cytochrome *c* on pure *trans-trans* methyl linoleate prepared as previously described[4] has now been studied. Working with a 5×10^{-3} *M* suspension of the pure hydroperoxide in a very weak solution of sodium dodecyl sulphate, it has been observed that cytochrome *c* at a concentration of $1{\cdot}6 \times 10^{-4}$ *M* will cause the almost instantaneous destruction of 80–90 per cent of the peroxide, and that about a third of the cytochrome is 'denatured' at the same time. Oxygen gas is not liberated during the reaction but there is a loss of conjugated di-ene unsaturation, just slightly less than the loss of peroxide. The reaction is not affected in any way by diluting the peroxide with an equal quantity of pure methyl linoleate, or by a change in *p*H over the range 5·8–8·0. Haematin and porphyrin *c* are both inactive; the former is slowly destroyed by the peroxide.

Work is continuing with the object of identifying the products of the reaction; in particular, it is hoped to identify the reduced hydroperoxide and to obtain further knowledge of the 'denatured' cytochrome *c*.

This work was carried out as part of the programme of the Department of Scientific and Industrial Research.

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[1] Banks, A., *Rep. Food Invest. Board*, 1939, 49 (1949).
[2] Tappel, A. L., *Food Res.*, **18**, 560 (1953).
[3] Banks, A., *J. Soc. Chem. Indust.*, **63**, 8 (1944).
[4] Banks, A., Fazakerley, S., Keay, J. N., and Smith, J. G. M., *Nature*, **184**, 816 (1959).

Isolation of Peptides containing Hydroxyproline from Animal Tissues

The idea that fibrogenic cells secrete peptide which, in extracellular spaces, is built into collagen fibre has been postulated repeatedly in the course of the past thirty years[1,2]. There is no direct evidence, so far, of the existence of a peptide which, as a precursor of collagen, should contain the typical collagen imino-acid hydroxyproline. Peptides containing hydroxyproline isolated from urine[3,4] can be considered rather as products of collagen catabolism than as steps in the course of biosynthesis of collagen.

In 1959 we found peptide-bound hydroxyproline in ultrafiltrates of extracts from different animal tissues; for elucidation of its biological significance we have presented some work[5–7] which favours the hypothesis that peptides represent non-protein precursors of collagen protein.

In this communication we give the results of experiments dealing with the isolation and identification of peptides containing hydroxyproline.

We have experimented mostly with the skin of 2–4-months-old pig embryos. Apart from that we have investigated the granulation tissue after the application of carrageenin under the skin of guinea pigs, and we have examined growth-zones of bones in bovine embryos. Results presented in this communication involve peptides from pig embryo skin.

Fresh tissue was homogenized, immediately after freezing with liquid air, by pulverization in a mortar and shaken in a mixture of ethanol and 0·5 per cent of acetic acid (3 : 1 v/v). The suspension warmed to boiling point was kept overnight at 0°. After centrifugation, the ethanol in the supernatant was removed by low-pressure distillation at a temperature not exceeding 20° and condensed by freeze-drying. For deproteination we used a metal ultrafilter with membrane 'Nojax' cellulose casings, Visking Corp., Chicago, at a pressure of 7 atm. approximately and a temperature of 1°. The ultrafiltrate was independent of the total ultrafilterable hydroxyproline condensed again by freeze-drying. Fractionation of ultrafiltrate was carried out first by column chromatography (100 cm. × 1 cm.), using 'Dowex 50 × 4', mesh 200 in ammonia cycle. The column was developed by passing the system through a solution of 0·2 *M* ammonium formate (*p*H 3·3) and 0·2 *M* ammonium acetate (*p*H 5·3) into the mixing chamber used for gradient elution at 20–30 ml./hr. and effluent was collected in 5-ml. fractions. Fractionation was followed by determining the content of free and bound hydroxyproline in different fractions. Bound hydroxyproline was ascertained from the difference in hydroxyproline

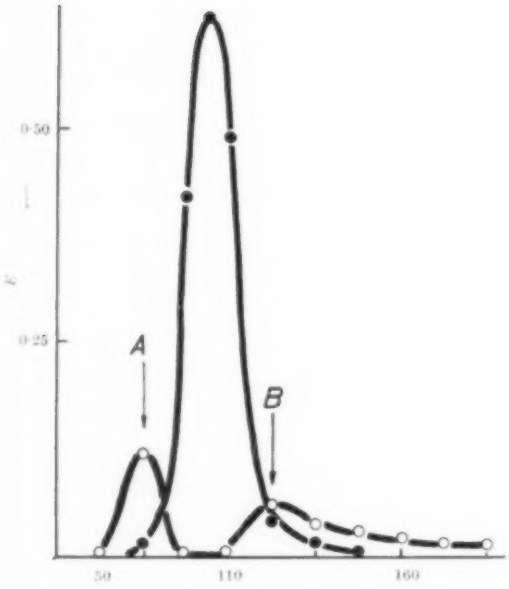

Fig. 1. Free hydroxyproline and peptide in ultrafiltrate of extract from pig embryo skin fractionated on 'Dowex 50 × 4'. ○, Peptide-bound hydroxyproline; ●, free hydroxyproline; the amount of hydroxyproline is given by extinction of sample.

content before and after acid hydrolysis of the sample (3 hr., 140°, 6 *N* hydrochloric acid). Fractions containing bound hydroxyproline were re-chromatographed on Whatman 4 (descending) in butanol/acetic acid/water (4 : 1 : 1). Peptides and amino-acids were detected by 0·1 per cent ninhydrin solution in acetone, by a specific method for detecting hydroxyproline[9] and after chloration of peptide bonds by iodostarch reagents. Strips of chromatograms containing peptides were eluted by water and re-chromatographed in a similar way. Hydroxyproline[10] and proline[11] were determined colorimetrically in aliquots of extract. The amino-acid composition of individual peptides was ascertained after acid hydrolysis, using paper chromatography as mentioned.

As shown in Fig. 1 with column chromatography, we found two fractions, *A* and *B*, with peptide hydroxyproline. By preparative paper chromatography we identified in fraction *A* at least four other peptides in which the content of proline and hydroxyproline was determined. It was found that molar relation of proline to hydroxyproline in individual peptides deviates from 5 : 1 to 1 : 1. Owing to the fact that the ratio of both imino-acids mentioned is 1 : 1 in mature mammal collagens, this finding is in good agreement with the generally accepted opinion, that hydroxylation of proline proceeds after its incorporation into peptide. Homogeneous spots of peptides A_1–A_4 obtained by re-chromatography were hydrolysed and the amount of amino-acid determined. The list of amino-acids is given in Table 1. This examination proved that peptides with greater mobility on paper chromatography contain a lower number of different amino-acids. But glycine, glutamic acid, proline and hydroxyproline were always found. Some spots have not been identified so far.

Table 1. Amino-acid Composition of Individual Peptides of Fraction *A*

A_1	A_2	A_3	A_4
Lys	Lys	Gly	Gly
Arg	Gly	Glu	Glu
Gly	Glu	Hypro	Hypro
Glu	Hypro	Ala	Pro
Hypro	Ala	Pro	
Ala	Pro		
Pro	Leu		
Val			
Leu			

Peptide hydroxyproline formed 20–30 per cent of total ultrafiltrable hydroxyproline.

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[1] Randall, J. T., *Nature and Structure of Collagen*, 232 (Butterworths Scientific Publications, London, 1953).
[2] Porter, K. R., and Pappas, G. D., *J. Biophys. Biochem. Cytol.*, **5**, 153 (1959).
[3] Ziff, M., Kibrick, A., Dresner, E., and Gribetz, H. J., *J. Clin. Invest.*, **35**, 579 (1956).
[4] Mechanic, G., Skupp, S. J., Safier, L. B., and Kibrick, A. C., *Arch. Biochem. Biophys.*, **86**, 71 (1960).
[5] Chvapil, M., and Čmuchalová, B., *Nature*, **186**, 807 (1960).
[6] Chvapil, M., Holečková, E., and Čmuchalová, B., *Exp. Cell Res.* (in the press).
[7] Chvapil, M., and Čmuchalová, B., *Exp. Med. and Surg.* (in the press).
[8] Winnick, T., Winnick, R. T., Acher, R., and Fromageot, C., *Biochim. Biophys. Acta*, **18**, 488 (1955).
[9] Stegemann, H., and Griffin, H. F., *Naturwiss.*, **45**, 263 (1958).
[10] Stegemann, H., *Z. physiol. Chem.*, **311**, 41 (1958).
[11] Chinard, F. P., *J. Biol. Chem.*, **199**, 91 (1952).

Demethylation in the Metabolism of (−)-Nicotine *in vivo*

The physiological disposition of nicotine randomly labelled with carbon-14 has been subjected to investigation by many authors[1–3]. After intravenous administration to mice[1] and to dogs[2] analyses of the expired air showed no radioactive carbon dioxide. In an extension of this work, in which degradation of nicotine was investigated, the methylamine fraction of dog urine was examined for radioactivity and found[2] to contain none.

If the foregoing results are accepted as being completely definitive for the metabolism of nicotine, the inevitable conclusion is that nicotine undergoes an unusual metabolism with no degradation to single-carbon metabolites. This conclusion would tend to contradict our work[4] in which demethylcotinine, 5-(3′-pyridyl)-pyrrolidone-2, has been identified in urine after administration of nicotine. The need for a direct experimental resolution of this apparent contradiction has led to our employment of labelled nicotine containing a high level of activity in the methyl group.

Nicotine-methyl-^{14}C was conveniently synthesized in high yield by methylating (−)-nornicotine with formaldehyde-^{14}C in the presence of formic acid. This methylation reaction has been previously employed as a quantitative analytical procedure[5].

Male albino rats, weighing approximately 250 gm. and housed in glass metabolism cages, received the labelled nicotine intraperitoneally (0·2 mgm./100 gm.). The approximate radioactivity of the dose was 24·8 × 10^3 c.p.m. Expired carbon dioxide was collected in sodium hydroxide traps and then precipitated as barium carbonate for counting at infinite thickness. Radioactivity was readily demonstrated in the expired air. During the first 6-hr. period after

administration of the nicotine, the respiratory carbon dioxide from three animals contained an average of 5·7 per cent of the administered radioactivity with individual values: 7·5, 4·0, and 5·6 per cent. Further elimination as radioactive carbon dioxide was observed in a subsequent 18-hr. period to give cumulative values of 12·8, 6·2 and 8·4 per cent of the administered dose. In addition, a small but significant amount of carbon-14 activity was present as urea (as determined from carbon dioxide evolved by urease) in the individual 24-hr. urines (0·26, 0·17, and 0·24 per cent).

The fact that previous workers did not obtain any indication that nicotine is degraded to carbon dioxide may be attributed to a lower level of methyl-^{14}C activity of the nicotine used in their experiments. Although our work with nicotine-methyl-^{14}C has not included any experiments on the dog, and does not indicate the precise point at which demethylation occurs, the fact that demethylcotinine arises from both (−)-nicotine and (−)-cotinine[4] in the dog points to the importance of single-carbon compounds in the metabolism of nicotine in this species.

Since the radioactivity of randomly labelled nicotine-^{14}C is excreted[2] to the extent of 94 per cent in the urine of rats, the addition of carbon-14 determined as carbon dioxide in our investigations gives a total elimination which approaches 100 per cent. This provides convincing evidence that, after single doses, storage of nicotine or its metabolites occurs to only an extremely limited extent.

We wish to thank the American Tobacco Co. and the Tobacco Industry Research Committee for generous support.

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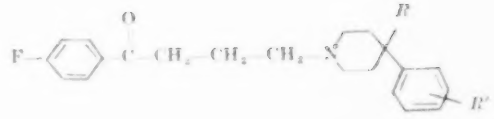
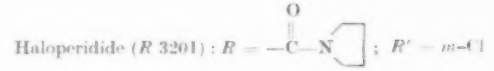
[1] Ganz, A., Kelsey, F. E., and Geiling, E. M. K., *J. Pharmacol. Exp. Therap.*, **103**, 209 (1951).
[2] Bennett, D. R., Tedeschi, R. E., and Larson, P. S., *Arch. int. Pharmacodyn.*, **98**, 221 (1954).
[3] Owen, jun., F. B., and Larson, P. S., *Arch. int. Pharmacodyn.*, **115**, 402 (1958).
[4] McKennis, jun., H., Turnbull, L. B., Bowman, E. R., and Wada, E., *J. Amer. Chem. Soc.*, **81**, 3951 (1959).
[5] Markwood, L. N., *J. Assoc. Off. Agric. Chemists*, **26**, 283 (1943).

Haloperidide (*R* 3201), a Highly Potent and Selective Anti-emetic Agent in Dogs

HALOPERIDIDE, the proposed generic name for 4′-fluoro-(4-(4′-pyrrolidin-amido-4′-*m*-chlorophenyl)-piperidino)-butyrophenone (serial number *R* 3201), was synthesized in the Organic Chemistry Department of this Laboratory. It is a new member of the butyrophenone series of neuroleptic compounds (Fig. 1). The prototype of this series, haloperidol (*R* 1625), has been described in a number of pharmacological and clinical publications. It has been shown that haloperidol is pharmacologically related to the potent neuroleptics of the phenothiazine-series[1–5].

Both haloperidol and perphenazine are potent inhibitors of the emetic effect of apomorphine in dogs[2,3,5]. After subcutaneous injection, haloperidol has a quicker onset and a considerably longer duration





Haloperidide (*R* 3201): $R = -C(=O)-N$; $R' = m$-Cl

Haloperidol (*R* 1625): $R = OH$; $R' = p$-Cl

of action than perphenazine, the estimated potency ratios varying considerably as a function of the time-interval between the injection of the drug and of the apomorphine challenging dose (Table 1). Haloperidide is considerably more active than either haloperidol or perphenazine in this test. It has a somewhat longer duration of anti-emetic action than perphenazine, but the onset of its effect is much shorter (Table 1).

Table 1. POTENCY RATIOS IN DOGS

Hr. after subcutaneous injection	Drug	*A* anti-emetic potency	*B* 'jumping box'	Ratio *A*/*B*
1–5	perphenazine	1	1	1
	haloperidol	1	4	1/4
	haloperidide	10	4	5/2
25–30	perphenazine	1	1	1
	haloperidol	4	6	2/3
	haloperidide	20	4	5

In an effort to evaluate the selectivity of these anti-emetic effects, we investigated the influence of the three drugs on avoidance and escape behaviour of trained dogs in a 'jumping box' situation. The details of the procedure, similar to the well-known Warner technique for rats, are described in a previous communication[6].

Briefly, the 'jumping box' consists of two compartments, separated by a partition. The floor of each compartment is a grill which can be charged electrically. The animal can escape shock or avoid it by jumping into the other compartment when presented with a warning signal (buzzer; maximum duration of 15 sec.). After adequate training, the dogs are treated at random at weekly intervals with selected doses of each compound, the effects on reaction-time, avoidance and escape being investigated 1, 5, 25 and 30 hr. after dosage.

The potency ratios in Table 1 are derived from two separate Latin square experiments. In one experiment four doses of haloperidol and four doses of haloperidide were investigated in eight dogs (8 × 8 design). In the other experiment six dogs were treated with three doses of haloperidol and three doses of perphenazine (6 × 6 design). The results obtained with all three substances are qualitatively similar. At low dose-levels, reaction times are prolonged. With increasing dosage, this effect leads to gradual and transient loss of learned avoidance and of escape behaviour.

It is concluded that haloperidide is a more potent, more selective, faster and longer acting antagonist of the emetic effects of apomorphine than perphenazine.

It is also more potent and more selective than haloperidol, but shorter acting.

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[1] Janssen, P. A. J., Jageneau, A. H. M., and Schellekens, K. H. L., *Psychopharmacologia*, **1**, 389 (1960).
[2] Janssen, P. A. J., and Niemegeers, C. J. E., *Arzneimittel-Forsch.*, **9**, 765 (1959).
[3] Janssen, P. A. J., Niemegeers, C. J. E., and Schellekens, K. H. L., *Arzneimittel-Forsch.*, **10**, 955 (1960).
[4] Janssen, P. A. J., van de Westeringh, C., Jageneau, A. H. M., Demoen, P. J. A., Hermans, B. K. F., Van Daele, G. H. P., Schellekens, K. H. L., Van der Eycken, C. A. M., and Niemegeers, C. J. E., *J. Med. Pharm. Chem.*, **1**, 281 (1959).
[5] Niemegeers, C. J. E., thesis, Paris (1960).
[6] Niemegeers, C. J. E., and Janssen, P. A. J., *J. Pharm. Pharmacol.*, **12**, 744 (1960).

Effect of Erythropoietine on Incorporation of Formate labelled with Carbon-14 into the Nucleic Acids of Normal Rabbit Tissues *in vitro*

It has previously been shown that the blood and urine of rabbits suffering from hæmolytic anæmia contain a mucoprotein humoral factor, hæmopoietine or erythropoietine, which on injection into normal animals stimulates erythropoiesis[1]. The present experiments were undertaken to find out what effect this factor might have on nucleic acid biosynthesis in normal rabbit tissues *in vitro*. A crude preparation of erythropoietine was obtained from the urine of animals made anæmic with phenylhydrazine. The urine was brought to *p*H 4·5 with hydrochloric acid, and 4 volumes of ethanol were added. After standing overnight at 4° C. the precipitate was centrifuged down, washed with ethanol and ether, and dried. The dry powder was extracted with a small volume of Krebs–Ringer bicarbonate buffer. The protein concentration of this 'anæmic urine extract' was determined by the biuret method. A 'normal urine extract' was similarly prepared from the urine of normal rabbits. The effects of both extracts on the incorporation of formate labelled with carbon-14 into the nucleic acids of bone marrow, spleen and liver *in vitro* were determined by the methods of Smellie *et al.*[2].

The results obtained are shown in Table 1. In agreement with results previously reported[3], the pattern of incorporation in normal bone marrow is characterized by the very high activity of the deoxyribonucleic acid thymine relative to the purines of both ribonucleic acid and deoxyribonucleic acid. In contrast, in spleen and liver deoxyribonucleic acid the activity of the thymine is generally only slightly greater than that of the purines. In previous papers[2,3] it has been argued that these observations may indicate that bone marrow, unlike the other tissues, may be incapable of synthesizing purine nucleotides fast enough to meet its own requirements. Bone marrow also differs from spleen and liver in its response to the urine extracts. The 'anæmic extract' produces virtually no effect on it, while the 'normal extract' tends to depress the activity of the nucleic acid purines and to a lesser extent, of the deoxyribonucleic acid thymine. In liver and spleen, on the other hand, the 'normal extract' has little or no effect, while the 'anæmic extract' causes a dramatic increase in the activity of the purines in both nucleic acids. In spleen, though not in liver, the anæmic extract also increases the activity of the deoxyribonucleic acid thymine.

These observations suggest that *in vivo* erythropoietine may stimulate *de novo* nucleic acid synthesis in liver and spleen, but not in bone marrow. However, Smellie *et al.*[4] have found that, in the rabbit, hæmolytic anæmia results in increased incorporation of $^{32}PO_4$ into the nucleic acids, not only of spleen, but also of bone marrow. An explanation of this latter observation may perhaps be found in the relationship between liver and bone marrow. Lajtha and Vane[5] have shown that *in vivo* hepatectomy greatly diminishes incorporation of ^{14}C-formate into the nucleic acid purines of rabbit bone marrow. Clearly, therefore, the liver must play some part in the synthesis of the purines which the bone marrow requires (for example, for nucleic acid synthesis), but which it cannot synthesize for itself. It is therefore quite possible that erythropoietine might stimulate erythropoiesis in the bone marrow indirectly by acting on the liver. The increased incorporation of ^{14}C-formate into liver nucleic acid purines produced by erythropoietine in the present experiments might be a reflexion of such action.

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Table 1. Incorporation of ^{14}C-formate* into Nucleic Acid Bases of Normal Rabbit tissues *in vitro*

Additions	Product analysed	Specific activity (counts/min./μmole)					
		Bone marrow		Spleen		Liver	
		RNA	DNA	RNA	DNA	RNA	DNA
Nil	Adenine	2,495	1,183	426	188	128	406
	Guanine	539	631	167	113	100	102
	Thymine		24,500		317		1,026
'Normal urine extract'†	Adenine	980	536	489	159	240	486
	Guanine	335	395	202	108	167	—
	Thymine		16,200		438		675
'Anæmic urine extract'†	Adenine	3,080	963	3,750	662	3,055	734
	Guanine	—	374	1,205	372	1,220	425
	Thymine		28,400		730		671

Incubation time, 4 hr. * Isotope concentration, 5 μc./ml. † Concentration of extracts, 2·3 mgm. protein/ml. RNA, ribonucleic acid; DNA, deoxyribonucleic acid.

[1] Hodgson, G., Perretta, M., Yudilevich, D., and Eskuche, I., *Proc. Soc. Exp. Biol. Med.*, **99**, 137 (1958).
[2] Smellie, R. M. S., Thomson, R. Y., and Davidson, J. N., *Biochim. Biophys. Acta*, **29**, 59 (1958).
[3] Thomson, R. Y., Perretta, M. A., and Ricceri, G., *Biochim. Biophys. Acta*, **45**, 87 (1960).
[4] Smellie, R. M. S., Humphrey, G. F., Kay, E. R. M., and Davidson, J. N., *Biochem. J.*, **60**, 177 (1955).
[5] Lajtha, L. G., and Vane, J. R., *Nature*, **182**, 191 (1958).

Adrenocorticotrophin and the Sugar-level in Plasma in Young Fowls

THIS communication is prompted by the finding of Urist and Deutsch[1] that large doses of freeze-dried adrenocorticotrophin of mammalian origin were without effect on the blood sugar of adult cocks (Black Minorcas) and hens (White Leghorns). Some years ago, work in this laboratory required the intramuscular injection of Brown Leghorn pullets and cockerels (5 weeks of age, body-weight 500 gm.) with large doses of long-acting adrenocorticotrophin ('Acthar', Armour). It was found that the hormone could produce a marked rise in the level of plasma sugar in these young birds, which were kept in brooders with free access to food and water throughout the experimental period.

Trichloroacetic acid filtrates of the plasma were analysed by my adaptation[2] of Jones and Pridham's method[3] (1954). Injections (0·5 ml.; 20 I.U.) of 'Acthar' were made into the pectoral muscle and the birds returned to the brooder. These injections were repeated on the two following days. The birds at no time showed signs of distress or lack of appetite. On the fourth day, blood was again taken for analysis; in some instances further samples were taken on the 5th, 8th and 18th days after the start of the experiment. Control birds were not injected.

The results are summarized in Table 1. While injection of adrenocorticotrophin was followed on the 4th day by a marked rise in the plasma sugar in seven out of eight experiments, by the 5th day the sugar had fallen to, if not below, the normal level. The responses of the two sexes were indistinguishable. It will be noted that the effect of the long-acting 'Achthar' was not observed 48 hr. after the last injection.

The present findings, along with those of others, on the effects of adrenocorticotrophin, raise the question whether the stage of development of the fowl is a factor in relation to the effects of the hormone. Urist and Deutsch[1] found no effect on the sugar-level of whole blood from adult birds when this hormone was administered, in contradistinction to mammalian species. Perek and Eckstein[4], and Perek and Eilat[5] showed that the adrenals of the young immature bird failed to respond to adrenocorticotrophin with respect to ascorbic acid depletion, again in contradistinction to the mammal, due to the activity of a lymphoepithelioid organ of as yet incompletely defined function, the bursa of Fabricius. This, situated at the dorsal aspect of the proctodæum, involutes during the approach to maturity. The ascorbic acid of the adrenal of the bursectomized chick is responsive to adrenocorticotrophin. (*Note added in proof.* H. S. Siegel and W. L. Beane (*Poultry Sci.*, **40**, 216; 1961) have also observed hyperglycæmia subsequent to intramuscular adrenocorticotrophin-gel in 6–7-week-old fowls.)

Drs. J. Beattie and J. G. Campbell and I find that bursectomy does not alter the positive response of the 5-week-old bird to long-acting adrenocorticotrophin. Adults, 24 hr. after 40 I.U., show 500–600 mgm. of reducing sugar per 100 ml. of plasma along with diuresis and glycosuria. On the other hand, I have so far failed to find any hyperglycæmic effect, on young intact and bursectomized birds, after freeze-dried adrenocorticotrophin.

Table 1. EFFECTS ON REDUCING SUGAR OF PLASMA OF INTRAMUSCULAR 'ACTHAR' GEL ON FIVE-WEEK-OLD PULLETS AND COCKERELS
Injections were given on days 1, 2 and 3

Exp. No.	Injection Days	Plasma reducing sugar (mgm./100 ml.)					
				Change			
		*D*1	*D*4	*D*1 to *D*4	*D*5	*D*8	*D*18
1	'Acthar'	205	240	+ 35	—	—	—
2		310	950	+ 640	—	—	—
3		270	680	+ 410	—	—	—
4		240	450	+ 210	—	—	—
5		295	670	+ 375	230	210	230
6		250	530	+ 280	210	225	220
7		275	410	+ 135	205	220	230
8		290	710	+ 420	200	200	220
—	Nil (controls)	220	250	+ 30	—	—	—
—		225	255	+ 30	—	—	—
—		240	235	− 5	—	—	—
—		250	240	− 10	—	—	—
—		230	230	0	—	—	—
—		230	235	+ 5	—	—	—
—		200	190	− 10	—	—	—
—		190	205	+ 15	—	—	—
—		190	200	+ 10	—	—	—

I have so far failed to find any hyperglycæmic effect, on young intact and bursectomized birds, after freeze-dried adrenocorticotrophin.

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[1] Urist, M. R., and Deutsch, N. M., *Proc. Soc. Exp. Biol. N.Y.*, **104**, 35 (1960).
[2] Bell, D. J., *Biochem. J.*, **66**, 137 (1956).
[3] Jones, J. K. N., and Pridham, J. B., *Biochem. J.*, **58**, 288 (1954).
[4] Perek, M., and Eckstein, B., *Poultry Sci.*, **38**, 996 (1959).
[5] Perek, M., and Eilat, A., *J. Endocrinol.*, **20**, 251 (1960).

Presence of Sialic Acid in a Granuloma Pouch

THE presence of sialic acid in connective tissues has already been described[1]. It is well known that by means of a granuloma pouch newly formed connective tissue can be induced; this is very important for the evolution of inflammation. The presence and the concentration of sialic acid in the granuloma pouch have now been investigated.

Granulomas were induced in 150 gm. male rats by the use of 10 ml. of air and 0·4 ml. of croton oil solution (4 per cent in olive oil). The animals were killed 1, 3, 5 and 8 days after treatment. The dissected granulomas were homogenized in acetone and stirred for 48 hr.; after centrifugation, the sediment suspended in ethyl ether was dried in vacuum. The powder so obtained was employed to determine nitrogen and sialic acid content by Svennerholm's method[2].

For the last determination the powder was hydrolysed with 0·1 *N* sulphuric acid at 80° C. for 1 hr.; the hydrolysate was filtered on a sintered glass filter and chromatographed on a 'Dowex 2 × 8' column; after elution with 1 *M* acetate buffer *p*H 4·6, the eluate was tested by the resorcinol reaction and sialic acid was identified by the absorption spectrum of the reaction.

A control determination was carried out using an untreated region of the abdomen (non-inflamed tissue).

Table 1. PRESENCE OF SIALIC ACID IN A GRANULOMA POUCH INDUCED IN RAT

Days after treatment	Values referred to 100 mgm. of acetonic powder: Granuloma pouch	Non-inflamed tissue
1	480 μgm.	96 μgm.
3	426 ,,	91 ,,
	473 ,,	78 ,,
5	319 ,,	
	386 ,,	
8	313 ,,	47 ,,
	343 ,,	

N-acetyl neuraminic acid, kindly supplied by Prof. G. Blix, was used as a standard to determine the sialic acid quantitatively. The results are presented in Table 1.

The results indicate that the content of sialic acid in a granuloma pouch is much greater than in a corresponding abdominal region not involved in the pathological process.

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[1] Castellani, A. A., Ferri, G., Bolognani, L., and Graziano, V., *Nature*, **185**, 37 (1960).
[2] Svennerholm, L., *Acta Chemica Scand.*, **12**, 547 (1958).

Content of Sialic Acid in Serous Glands of Equines

In histochemistry it is well known that an objection to the specificity of the periodic acid–Schiff reaction for mucopolysaccharides is due to the possible interference of some amino-acids. This objection is particularly important when the periodic acid–Schiff reaction is applied to serous glands, in which the secretion is essentially proteins. However, Junqueira *et al.*[1] found material giving a positive reaction in the parotids of many mammals, and concluded that substances other than proteins were present in the secretion of parotid gland. This observation opened up an interesting problem of cellular biology, regarding the possibility of a multiple secretion from serous glands.

In order to confirm this observation, a comparative histochemical investigation of material positive to the periodic acid–Schiff reagent and the ribonucleic acid content of some serous glands was carried out by Bignardi *et al.*[2]. This investigation, using pancreas, parotid and orbital glands of equines, demonstrated that the intensity of periodic acid–Schiff reaction varied inversely with the ribonucleic acid content. On the basis of general views on the function of ribonucleic acid in protein biosynthesis, this result was interpreted as indirect evidence that positive reaction to the periodic acid–Schiff reagent was really due to carbohydrate material.

Since more direct evidence for this view could be obtained by chemical analysis of some constituent of mucopolysaccharides, we have investigated the content of sialic acid in serous glands. The emphasis on sialic acid was due to its presence in submaxillary mucin[3] and to its strong reactivity for periodic acid. (In a very recent paper of Quintarelli *et al.*[4], a relation between sialic acid and positive periodic acid–Schiff reaction has been reported.)

Sialic acid has been determined in orbital glands (lacrimal gland and gland of the third eyelid), parotid and pancreas of ass and horse.

The glands were removed and stored under acetone. About 50 mgm. (dry tissue) of each gland was used for sialic acid determination, which was carried out by Svennerholm's method[5]. The tissue was homogenized with 5 ml. of 0·1 *N* sulphuric acid by Potter–Elvehjem homogenizer and refluxed at 80° C. for 1 hr. The hydrolysate was centrifuged and the supernatant chromatographed on 'Dowex 2 × 8'; the sialic acid was eluted by acetate buffer 0·1 *M*, *p*H 4·6, and sialic acid determined by the resorcinol reaction.

Table 1. Content of Sialic Acid in Serous Glands of Equines
(Values are referred to 100 mgm. of dry tissue)

Animals	Lacrimal gland	Gland of the third eyelid	Parotid	Pancreas
Ass 1	500 μgm.	410 μgm.	195 μgm.	118 μgm.
2	420 „	362 „	167 „	127 „
3	430 „		181 „	
Horse*				
1	621 μgm.	408 μgm.	157 μgm.	134 μgm.
2	778 „	427 „	138 „	168 „

* The presence of sialic acid in parotid gland of the horse has been reported by Svennerholm (ref. 5).

The standard curve was obtained with *N*-acetyl-neuraminic acid isolated from sheep submaxillary gland and kindly supplied to us by Prof. G. Blix. The results are reported in Table 1.

The results show that the highest content of sialic acid is in the orbital glands, a low content in parotid and the lowest in pancreas. Since positive periodic acid–Schiff reaction is also highest in glands of the orbit, is less in the parotid and is weakly positive in the pancreas, there seems to be a relation between the periodic acid–Schiff reaction and sialic acid content.

The presence of sialic acid and, probably, of a sialopolysaccharide, in serous glands shows that these glands elaborate not only protein but also carbohydrate material.

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[1] Junqueira, L. C. U., and Hirsch, G. C., *Int. Rev. Cytol.*, 323 (1956).
[2] Bignardi, C., Aureli, G., and Rizzotti, M., *Ric. Istochem. Norm. Pat.*, **6**, 167 (1960).
[3] Blix, G., *Hoppe-Seylers Z. physiol. Chem.*, **240**, 43 (1936).
[4] Quintarelli, G., Tsuiki, S., Hashimoto, Y., and Pigman, W., *Biochem. Biophys., Research Comm.*, **2**, 423 (1960).
[5] Svennerholm, L., *Acta chemica Scand.*, **12**, 547 (1958).

In vivo Metabolism of N-Acetylhexosamine ^{35}S-Sulphate Esters

In a previous report[1] evidence was presented indicating that the monosulphate ester obtained as the principal product of the direct sulphation of N-acetyl-D-glucosamine with chlorosulphonic acid was identical with N-acetyl-D-glucosamine 6-O-sulphate prepared by definitive synthesis. In addition, following preliminary observations on the structure of the monosulphate ester prepared by the direct sulphation of N-acetyl-D-galactosamine[1], independent results from work on tritylation (triphenylmethylation)[2], and infrared spectroscopy[3,4], indicate that this material is also a 6-O-sulphate ester. Since available information suggests that N-acetyl-D-glucosamine 6-O-sulphate and N-acetyl-D-galactosamine 6-O-sulphate exist *in vivo* as part of the polymer chains of keratosulphate and chondroitin sulphate-C respectively[5,6], it was of interest to examine the *in vivo* metabolism of these N-acetylhexosamine sulphate esters.

The direct action of chloro-^{35}S-sulphonic acid on N-acetyl-D-glucosamine and N-acetyl-D-galactosamine yielded in each case a mixture of the mono-^{35}S-sulphate derivative together with the di-^{35}S-sulphate and unchanged parent compounds[1]. These preparations were fractionated by zone electrophoresis on

Table 1. Distribution of Radioactivity in Rat Urine, Fæces and Carcase after the Injection of *N*-Acetyl-D-Glucosamine 6-O-^{35}S-Sulphate

Results (expressed as percentage of the injected dose) are average values for 3 animals in each instance. The radioactivity of the doses corresponded to $1{\cdot}3 \times 10^7$ counts/min. (10 mgm.) and $2{\cdot}6 \times 10^7$ counts/min. (20 mgm.) measured after hydrolysis as an 'infinitely thick' plate of $Ba^{35}SO_4$

Sex	Dose (mgm.)	Distribution in urine: Inorganic sulphate fraction 24 hr.	48 hr.	72 hr.	96 hr.	Combined inorganic and ester sulphate fraction 24 hr.	48 hr.	72 hr.	96 hr.	Distribution in fæces 24 hr.	48 hr.	72 hr.	96 hr.	Residual ^{35}S in carcase after 96 hr.
Male	10	7·2	2·1	1·3	0·6	89·5	2·7	1·9	0·9	0·3	0·1	0·07	0·02	3·1
Male	20	5·3	3·2	1·9	1·1	90·8	4·4	2·8	1·6	0·2	0·1	0·09	0·04	1·7
Female	20	4·9	2·4	1·0	0·8	91·2	3·2	1·4	1·2	0·2	0·14	0·06	0·04	2·5

Table 2. Distribution of Radioactivity in Rat Urine, Fæces and Carcase after the Injection of *N*-Acetyl-D-Galactosamine 6-O-(^{35}S) Sulphate

Results (expressed as percentage of the injected dose) are average values for 3 animals. The radioactivity of the doses corresponded to $1{\cdot}8 \times 10^7$ counts/min. (10 mgm.) and $3{\cdot}6 \times 10^7$ counts/min. (20 mgm.) measured after hydrolysis as an 'infinitely thick' plate of $Ba^{35}SO_4$

Sex	Dose (mgm.)	Distribution in urine: Inorganic sulphate fraction 24 hr.	48 hr.	72 hr.	96 hr.	Combined inorganic and ester sulphate fraction 24 hr.	48 hr.	72 hr.	96 hr.	Distribution in fæces 24 hr.	48 hr.	72 hr.	96 hr.	Residual ^{35}S in carcase after 96 hr.
Male	10	5·6	2·7	1·1	0·3	87·3	3·1	1·5	0·7	0·41	0·15	0·08	0·03	4·2
Male	20	4·4	2·6	1·5	0·9	93·8	2·9	2·1	1·3	0·27	0·07	0·02	—	2·8
Female	20	5·2	1·9	1·7	0·5	92·9	2·3	2·5	0·8	0·38	0·11	0·04	0·01	2·6

cellulose columns[2] and the 6-O-^{35}S-sulphate esters finally isolated as the potassium salts. Chromatography of the products on Whatman No. 1 filter paper using downward irrigation with butan-1-ol/acetic acid/water, 50 : 12 : 25 (by vol.) or *iso*butyric acid/0·5 *N* ammonium hydroxide, 5 : 3 (by vol.) showed that each contained only a single component. The *N*-acetyl-D-glucosamine ester labelled with sulphur-35 was identical in chromatographic mobility with authentic *N*-acetyl-D-glucosamine 6-O-sulphate in both the solvents named above.

Male and female M.R.C. hooded rats (aged 2–3 months and weighing 130–150 gm.) were injected intraperitoneally with aqueous solutions of the labelled esters. The animals were housed separately in the funnel-type of metabolism cage and the urine and fæces collected at 24-hr. intervals up to 96 hr. Samples of the urine and fæces were taken for the determination of radioactivity according to Dodgson and Tudball[7]. At the end of the experimental period the animals were killed by a blow on the back of the head and the carcase used for the determination of retained radioactivity. The results of these experiments are recorded in Tables 1 and 2.

The striking feature of the metabolism of both *N*-acetyl-D-glucosamine 6-O-^{35}S-sulphate and *N*-acetyl-D-galactosamine 6-O-^{35}S-sulphate is the rapid elimination of radioactivity, 87–94 per cent of the injected doses appearing in the combined inorganic and ester sulphate fraction of urine in the 24-hr. period immediately following administration. The appearance of 9·0–11·5 per cent of the dose as inorganic ^{35}S-sulphate in the urine during the 96-hr. period after the injection of both esters is also of interest since it supports previous observations of the release of inorganic ^{35}S-sulphate in the urine of rats following the administration of labelled polysaccharides containing *N*-acetylhexosamine ^{35}S-sulphate residues[8,9]. It was found that radioactivity was retained in the carcase after 96 hr. in all instances. However, in view of the appearance of inorganic ^{35}S-sulphate in the urine, it is not possible to differentiate between the specific uptake of the intact labelled esters into the keratosulphate and chondroitin sulphate-C fractions of rat and a general incorporation of inorganic ^{35}S-sulphate into all the ester sulphates of rat tissues. A detailed account of these and other observations will be given elsewhere.

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[1] Lloyd, A. G., *Nature*, **183**, 109 (1959).
[2] Lloyd, A. G., *Biochem. J.*, **75**, 478 (1960).
[3] Lloyd, A. G., and Dodgson, K. S., *Nature*, **184**, 548 (1959).
[4] Lloyd, A. G., and Dodgson, K. S., *Biochim. Biophys. Acta*, **46**, 116 (1961).
[5] Hirano, S., Hoffman, P., and Meyer, K., *Fed. Proc.*, **19**, 146 (1960).
[6] Meyer, K., *Molecular Biology*, 69 (Academic Press, Inc., London, 1960).
[7] Dodgson, K. S., and Tudball, N., *Biochem. J.*, **74**, 154 (1960).
[8] Dohlman, C. H., *Acta Physiol. Scand.*, **37**, 220 (1956).
[9] Dziewiatkowski, D. D., *J. Biol. Chem.*, **223**, 239 (1956).

Identification of Sugars in the Manna of Northern Iraq

Manna is found in the Middle East in the Sinai peninsula and in Northern Iraq. Bodenheimer and Theodor[1] claimed that the manna they found on the leaves of *Tamarix* in Sinai is the excretion of the scale insects *Trabutina mannipara* and *Najacoccus serpentinus*. However, it is generally believed in northern Iraq (Allos, H. F., private communication) that manna is an exudate of *Fraxinus ornus* L. (West, W. A., private communication), probably from insect-produced wounds. The exudate usually accumulates on the leaves until they fall to the ground. The sugars are extracted from the raw material with boiling water and mixed with eggs to make a popular dessert. While sucrose and invert sugar have been identified in manna collected from Sinai[2], the Iraqi manna was shown to contain sucrose and melezitose[3] as well as trehalose[4].

Table 1. IDENTIFICATION OF SUGARS IN MANNA

Fraction		R_g values*		Response to reagents†						Hydrolysis products‡	Identity of Unknown
				I	II	III	IV	V	VI		
Monosaccharides	1	Unknown	112	*bn*	+	+	+	–	–		Fructose
		St'd fructose	111								
	2	Unknown	98	*b*	–	–	–	–	+		Glucose
		St'd glucose	100								
Disaccharides	3	Unknown	88	*bn*	–	–	+	–	–	Glucose + fructose	Sucrose
		St'd sucrose	85								
	4	Unknown	80	*b*	–	–	–	–	–	Glucose	Trehalose
		St'd trehalose	78								
Trisaccharides	5	Unknown	50	*g–bn*	–	+	+	–	–	Glucose + galactose + fructose	Raffinose
		St'd raffinose	53								
	6	Unknown	36	*g–bn*	–	–	+	–	–	Glucose + fructose	Melezitose
		St'd melezitose	36								
Polysaccharides	7	Unknown	—	–	–	–	–	–	–	Glucose	—

* Chromatograms were developed in butanol/pyridine/water (2 : 2 : 1); other developers gave comparable results.
† I, Aniline–diphenylamine (*b*, blue; *bn*, brown; *g*, grey; II, silver nitrate; III, 2 : 4-dinitrophenylhydrazine; IV, phloroglucinol; V, vanillin; VI, ammonium molybdate.
‡ These were identified by their R_g values and response to above-mentioned reagents.

Samples of manna collected in the Suleimaneyeh District in northern Iraq were kindly supplied to us by Dr. H. F. Allos. The sticky mass was dark grey in colour and contained some soil particles and leaf residues. Approximate analysis showed it to contain 5·9 per cent moisture, 0·2 per cent fat, 2·8 per cent protein, 5·2 per cent ash, 6·7 per cent fibre and 79·2 per cent carbohydrates (by difference).

The sugars were extracted from the manna with hot 80 per cent ethanol and the extract was desalted on 'Amberlite' resins '*IR*–120' and '*IRA*–410', then concentrated under vacuum to a thick syrup. The extract was chromatographed on a charcoal column, according to Whistler and Durso[5] and mono-, di- and tri-saccharides were eluted with water, 5 and 15 per cent ethanol, respectively. The adsorbent was then treated with 30 per cent ethanol to elute polysaccharides. Each of the four fractions was concentrated under vacuum and chromatographed on Whatman No. 4 paper strips (4 cm. × 60 cm.). The di-, tri- and poly-saccharide fractions were hydrolysed by refluxing with 50 volumes of *N* sulphuric acid for 6 hr., neutralizing with solid barium carbonate to congo red paper, centrifuging and chromatographing the supernatant. Paper chromatography was also carried out on the sugar extract from the manna.

The sugar constituents of the manna were identified according to:

(1) Their R_g values as compared with those of standard sugars and sugar derivatives developed simultaneously. The following developers were used and gave comparable results: 2-propanol/water (4 : 1), 2-propanol/pyridine/acetic acid/water (8 : 8 : 1 : 4), propanol/ethyl acetate/water (7 : 1 : 2), butanol/pyridine/water (2 : 2 : 1), phenol/water (4 : 1) and ethylacetate/pyridine/water (2 : 1 : 2).

(2) Specific reactions of sugars and sugar derivatives on the chromatogram:

(I) Aldoses and ketoses by aniline–diphenylamine spray, according to Buchan and Savage[6].

(II) Reducing sugars by the silver nitrate reagent described by Trevelyan and his associates[7].

(II) Fructose, sucrose and raffinose by spraying with saturated solution of 2,4-dinitrophenylhydrazine[8].

(IV) Ketoses by phloroglucinol–trichloroacetic acid mixture according to Horrocks and Manning[9].

(V) Sugar alcohols by vanillin–perchloric acid reagent[10].

(VI) Phosphate esters by ammonium molybdate spray[11].

The results indicate the presence of glucose, fructose, sucrose, trehalose, raffinose and melezitose, as shown in Table 1. While the polysaccharide fraction hydrolysed into glucose only, it gave no colour with iodine and showed no reducing power.

It is of interest to note that with the exception of glucose and fructose, which together constitute about 10 per cent of the carbohydrates in manna, all the other sugars are non-reducing.

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[1] Bodenheimer, F. S., and Theodor, O., *Ergebn. Sinai Expedition 1927 der Hebraischen Universität, Jerusalem*, 45 (Leipzig, 1929).
[2] Fodor, A., and Cohn, R., *Ergebn. Sinai Expedition 1927 der Hebraischen Universität, Jerusalem*, 89 (Leipzig, 1929).
[3] Colin, H., and Belval, H., *Bull. Assoc. Chem.*, **54**, 12 (1937).
[4] Leibowitz, J., *Biochem. J.*, **38**, 205 (1944).
[5] Whistler, R. L., and Durso, D. F., *J. Amer. Chem. Soc.*, **72**, 677 (1950).
[6] Buchan, J. L., and Savage, R. I., *Analyst*, **77**, 4015 (1952).
[7] Trevelyan, W. E., Procter, D. P., and Harrison, J. S., *Nature*, **166**, 444 (1950).
[8] Gray, R. A., *Science*, **115**, 129 (1952).
[9] Horrocks, R. H., and Manning, G. B., *Lancet*, I, 1042 (1949).
[10] Godin, P., *Nature*, **174**, 134 (1954).
[11] Hanes, C. S., and Isherwood, F. A., *Nature*, **164**, 1107 (1949).

Molecular Mechanisms for Hydrolytic Enzyme Action

FROM kinetic and other studies of hydrolyses catalysed by enzymes several important conclusions have emerged. One of these, coming particularly from *p*H studies, is that both an acid (*–A–H*) and a basic (*–B*) group are in some way involved in the reaction. A second conclusion is that there are two reaction intermediates, an addition (Michaelis) com-

plex (ES) and an acylated enzyme (ES'), so that the process may be represented as:

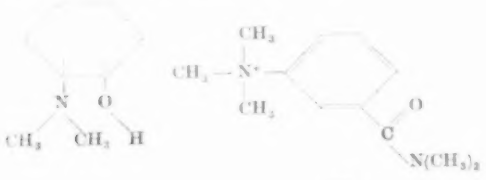
$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} ES' \xrightarrow{k_3} E + P_2 \\ + P_1$$

The site that becomes acylated has been a matter of some controversy, both imidazole and serine being possibilities.

We have recently carried out a series of investigations on the enzyme acetylcholinesterase, and have studied the effects of pH changes and of various inhibitors. On the basis of a kinetic analysis, the details of which will be published elsewhere, we have arrived at certain conclusions which seem to be consistent with the results for other enzyme systems. These conclusions relate to the detailed configuration of the active centre of the enzyme and to the way in which the substrate and inhibitors interact with the various components of the active centre. Acetylcholinesterase has an important advantage from the point of view of elucidating these problems owing to its possession of an anionic site which serves as an 'origin' from which distances to other parts of the active centre can be deduced.

By working with two substrates, for one of which $k_2 > k_3$ and for the other $k_3 > k_2$, it has proved possible to separate effects on ES from those on ES'. Proceeding in this way, so far as pH changes are concerned, we find that the basic group on the free enzyme has a pK of 6·5 and the acid group one of 9·3. In the Michaelis complex ES the basic group is no longer able to add on a proton at pH 6·5, but in the acyl enzyme ES' the proton can be added on at about this pH. The group of pK 6·5 is believed to be the imidazole group, and our conclusion is that this group interacts with the carbonyl group of the substrate in the Michaelis complex, but does not do so in the acyl enzyme. There must therefore be a transfer of the carbonyl group to another group, presumably serine, during the process $ES \rightarrow ES'$.

There are two types of inhibitor for this enzyme; those of the first class, which is exemplified by *cis*-2-dimethylaminocyclohexanol (I), give inhibition of the mixed competitive and non-competitive types, whereas those of the second, of which prostigmine (II) is an example, show pure competitive inhibition.



(I) (II)

In (I) the distance between the nitrogen atom and the OH group is about 2·5 Å., whereas in (II) the distance between the nitrogen atom and the carbonyl carbon atom is about 5 Å. The difference between competitive and non-competitive inhibition is conventionally ascribed to differences in binding of inhibitor to the enzyme-substrate complex; but this interpretation is excluded by our kinetic results for this system. We find that inhibitors of both classes can become attached to E and to ES' but not to ES. The difference between the types is that inhibitors of type I block the deacetylation reaction, whereas those of type II do not do so.

Support for this conclusion is provided by work we have done on the effects of the various inhibitors on the inhibition by substrate that is found with this enzyme. The results show that substrate inhibition is due not to the formation of a complex in which two substrate molecules are attached to the enzyme, but to the attachment of a substrate molecule to the acetyl enzyme with blocking of the deacetylation process. It can be shown from the steady-state equations that if an inhibitor blocks deacetylation the square of the concentration of substrate, $[S]_{opt.}$, corresponding to the maximum velocity, should vary linearly with [I]; if it does not, $[S]_{opt.}$ itself should vary linearly with [I]. These predictions have been confirmed for inhibitors of each type, studied by Augustinsson[2], Augustinsson and Nachmansohn[3], and ourselves.

These facts lead to a clear-cut picture of the active centre of the enzyme and of the course of reaction. We conclude that when type I inhibitors become attached to the free enzyme they do so at the anionic site and at the acid (A–H) site, a hydrogen bond being formed between the hydrogen of the acid site and the oxygen atom on the inhibitor. The presence of the substrate prevents a similar attachment in ES, but since in ES' the acyl group of the substrate has become transferred to serine a two-point attachment of the inhibitor is now possible. Since deacetylation is now blocked, the hydrogen atom of the acid site must be required for this process.

In type II inhibitors the attachment to the free enzyme is at the anionic site and at the imidazole nitrogen, which forms an electrostatic bond with the C=O dipole of the inhibitor. Again, no attachment to ES is possible. For ES' we conclude that attachment is only at the anionic site; the acyl group on the serine prevents attachment at the imidazole nitrogen. Since the inhibitor does not interact with the hydrogen atom of the acid site there is no inhibition of deacetylation.

These facts, and the deductions from them, lead to the picture of the active centre shown in Fig. 1. The acid and basic sites are situated 2·5 Å. and 5·0 Å. respectively from the anionic site, and the serine OH group is somewhat farther away. The figure also shows how, in our view, the substrate becomes attached to the enzyme. A more detailed

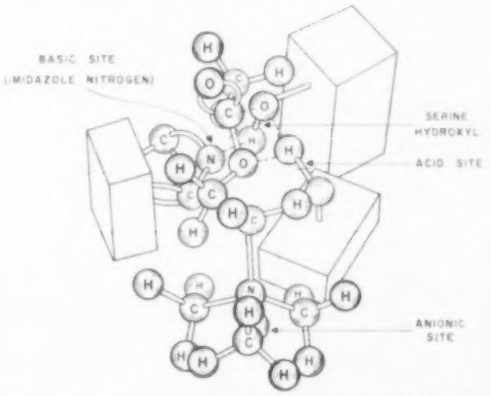


Fig. 1. Proposed arrangement of functional groups at the active centre of acetylcholinesterase. The substrate is shown in position, and electrostatic attractions occur at the dotted lines and also between the imidazole nitrogen atom and the carbonyl carbon atom. The dotted lines also indicate bonds formed during the acetylation process; the three bonds broken are marked on the diagram

discussion of the mechanism of the acetylation and deacetylation processes has been given elsewhere[4].

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[1] Wilson, I. B., and Bergmann, F., *J. Biol. Chem.*, **185**, 479 (1950). Wilson, I. B., *ibid.*, **197**, 215 (1952).
[2] Augustinsson, K.-B., *Acta Physiol. Scand.*, **15**, Supp. 52 (1948).
[3] Augustinsson, K.-B., and Nachmansohn, D., *J. Biol. Chem.*, **179**, 543 (1949).
[4] Krupka, R. M., and Laidler, K. J., *J. Amer. Chem. Soc.*, **83**, 1458 (1961).

PHYSIOLOGY

Spontaneous Potentials from Explants of Human Adult Cerebellum in Culture

Using techniques and supernatant similar to those used to demonstrate spontaneous potentials from explants of chick embryo cerebellum in tissue culture in Kahn tubes[1], spontaneous potentials have been demonstrated in explants from the surface of the upper postero-lateral aspects of human adult cerebellum. The explants were thin slices of the full thickness of cerebellar grey matter together with some of the related white matter. The control used was dead chick cerebellar tissue, side by side with the living culture material in the same incubator, with identical amplification and recording apparatus. The living brain tissue gave the same form and magnitude of potentials on any recording channel which was tried. The form of the potentials is shown in Figs. 1 and 2. Fig. 1 shows the typical activity after 12 hr. in culture. This consists of pairs of potentials having a complex wave-form. The first of the potentials in each pair has a magnitude of 75 μV. and the other, which follows after an interval of 12–15 sec., has about one-third of this potential. The interval between the pairs of spikes is about 45 sec. Fig. 2 shows the typical activity after 24 hr. in culture. The pairing of the spikes is much less common, and when it does occur the interval between the two members of the pair is very irregular. The interval between the potentials is more irregular and varies about 20 sec. The potentials at this time have a magnitude of about 20 μV. The culture continued to have spontaneous electrical activity until more than 72 hr. after explantation. No record of spontaneous potentials from adult brain in culture have been found in the literature. Further investigations of these potentials are in progress.

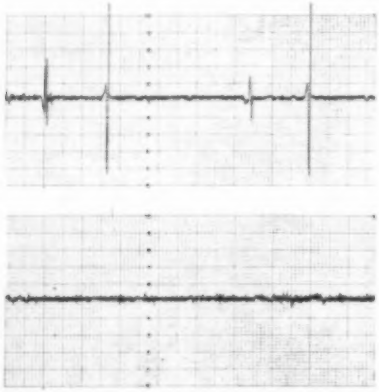

Fig. 1. Upper trace, spontaneous potentials from an explant of adult human cerebellum 12 hr. after explantation. Vertical lines 1 sec. apart; amplitude scale—distance between two horizontal lines equals 1½ μV. Lower trace, control of dead cerebellar tissue under identical conditions and with identical time and amplitude scales

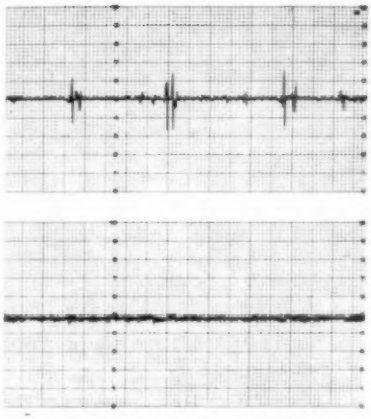

Fig. 2. Upper trace, spontaneous potentials from an explant of adult human cerebellum 24 hr. after explantation. Vertical lines 1 sec. apart; amplitude scale—distance between two horizontal lines equals 1½ μV. Lower trace, control of dead cerebellar tissue under identical conditions and with identical time and amplitude scales

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[1] Cunningham, Dougherty and Rylander, *Nature*, **186**, 477 (1960).

Assay of 5-Hydroxytryptophan Decarboxylation in Intact Brain

Intraperitoneal injection of 5-hydroxytryptophan (5HTP) shortly before death causes a considerable post-mortem rise of 5-hydroxytryptamine (5HT) in the brain of rats. This may be explained by the fact that 5HTP decarboxylation continues during the first few hours post-mortem whereas monoamine degradation by monoamine oxidase is probably considerably reduced[1]. In the work reported here the question was investigated whether this 5HTP induced post-mortem increase of brain 5HT might be used as a test for decarboxylase inhibitions. D,L-α-Methyl dihydroxyphenylalanine (α-methyl DOPA)[2–6] served as a model inhibitor.

Male Wistar rats weighing 60–80 gm. and fasted for 16 hr. were given 75 mgm. D,L-5HTP/kgm. by subcutaneous injection ½ hr. before decapitation. The 5HT content was determined by a spectrophotofluorometric method[7]: (*a*) in brain homogenized in 0·1 *N* hydrochloric acid immediately after death; (*b*) 2 hr. after incubation of the severed heads at 37° C. in small closed wet chambers. The 5HT difference between group (*a*) and (*b*) served as a measure for decarboxylase activity. α-methyl DOPA was injected intraperitoneally at various intervals before decapitation and the post-mortem rise of 5HT compared with that of controls.

In 5HTP pretreated rats the level of brain 5HT measured immediately after decapitation was 1·00 ±

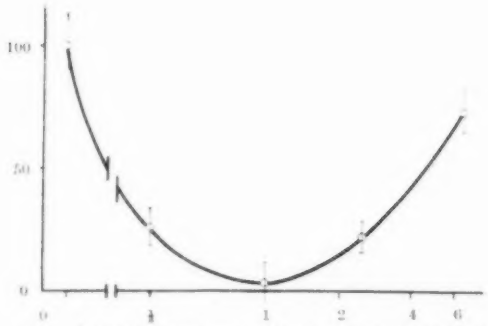

Fig. 1. Inhibition of post-mortem decarboxylation of 5-hydroxytryptophan (5HTP) by D,L-α-methyl dihydroxyphenylalanine (α-methyl DOPA) in intact rat brain in relation to time. Abscissa, hours after intraperitoneal injection of 105 mgm./kgm. α-methyl DOPA (logarithmic scale); ordinate, percentage 5-hydroxytryptamine (5HT) increase during the first 2 hr. after decapitation as compared with animals not receiving α-methyl DOPA. Subcutaneous injection of 75 mgm./kgm. D,L-5HTP ½ hr. prior to decapitation. Each point represents average and standard error of nine 5HT determinations

0·06 γ/gm. (controls 0·63 ± 0·02 γ/gm. 5HT). Incubation of the severed heads at 37° C. caused a further increase of 5HT of 0·86 ± 0·10 γ/gm. (considered as 100 per cent). α-methyl DOPA inhibited the post-mortem increase of 5HT considerably. The dose-dependent effect was maximal after 1 hr. and almost completely abolished after 6 hr.; 50 per cent inhibition was obtained by about 25 mgm./kgm. within 1 hr. (Figs. 1 and 2).

These findings show that the 5HTP induced post-mortem rise of 5HT is suitable for the investigation of decarboxylase inhibitors in brain. The results are in agreement with those obtained by measurement of decarboxylase activity in brain homogenates after injection of α-methyl DOPA into mice[6]. This method has the following advantages:

(1) Decarboxylase exerts its action in intact brain and not in disintegrated and diluted tissue (homogenates, supernatant, etc.).

(2) Monoamine oxidase activity does not interfere to any great extent, since under the almost anaerobic conditions post mortem it is nearly completely abolished[1]. Pharmacological inhibition of monoamine oxidase (for example, with iproniazid) is not necessary for the measurement of decarboxylation.

(3) The sensitivity is probably superior to that obtained by measurement of endogenous 5HT in brain. In the post-mortem method with rat brain 50 per cent decarboxylase inhibition can be obtained by about 25 mgm. α-methyl DOPA. A slight but significant decrease of endogenous 5HT in mouse brain, however, becomes evident only after 100 mgm./kgm. of the inhibitor[1].

Investigations on the decarboxylation of dihydroxyphenylalanine using the post-mortem method described are under way.

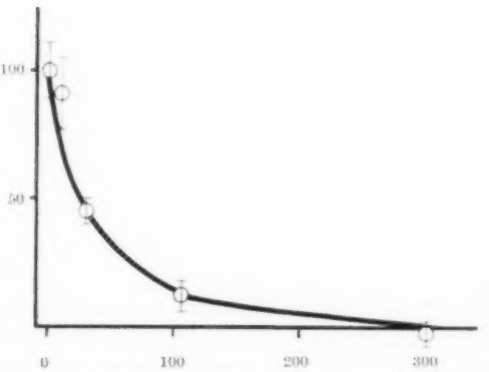

Fig. 2. Inhibition of post-mortem 5-hydroxytryptophan (5HTP) decarboxylation in intact rat brain, by D,L-α-methyl dihydroxyphenylalanine (α-methyl DOPA) in relation to dose. Abscissa, dose of α-methyl DOPA in mgm./kgm.; ordinate, percentage 5-hydroxytryptamine (5HT) increase within 2 hr. after decapitation as compared with animals not receiving α-methyl DOPA. Intraperitoneal injection of α-methyl DOPA 1 hr., subcutaneous injection of 75 mgm./kgm. D,L-5HTP ½ hr. before decapitation. Each point represents average and standard error of 5–11 5HT determinations

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[1] Gey, K. F., and Pletscher, A., *Experientia* (in the press).
[2] Sourkes, T. L., *Arch. Biochem.*, **51**, 444 (1954).
[3] Westermann, E., Balzer, H., and Kuell, J., *Naunyn-Schmiedeberg's Arch. Exp. Path. Pharmakol.*, **234**, 194 (1958).
[4] Sourkes, T. L., and Murphy, G. F., *Fed. Proc.*, **19**, 295 (1960).
[5] Oates, J. A., Gillespie, L., Udenfriend, S., and Sjoerdsma, A., *Science*, **131**, 1890 (1960).
[6] Smith, S. E., *Brit. J. Pharmacol.*, **15**, 319 (1960).
[7] Bogdanski, D. F., Pletscher, A., Brodie, B. B., and Udenfriend, S., *J. Pharmacol. Exp. Therap.*, **117**, 82 (1956).

Sodium Transport and Oxygen Consumption in the Mammalian Kidney

In the isolated frog skin, it was found by Zerahn[1] and by Leaf and Renshaw[2] that the amount of sodium actively transported had a fixed relationship to the net oxygen consumption (sodium/net oxygen ratio), as about 18 sodium ions were transported per molecule of oxygen consumed under a variety of experimental conditions. Net oxygen consumption was defined as the difference between the total oxygen uptake and the basal uptake, that is, the oxygen uptake when no sodium transport took place. In the mammalian kidney, active re-absorption of sodium (anions and water following passively) represents on a molar basis the overwhelming part of all tubular transport processes. On the assumption that sodium re-absorption does therefore require the bulk of the oxidative energy supplied, we have determined the sodium/net oxygen ratio in the intact kidney of the dog.

The basal oxygen consumption of the dog kidney, here defined as the oxygen consumption when no filtration and hence no re-absorption take place, was determined in four anæsthotized dogs during hypotension induced by bleeding. The absence of filtration was evident from an inulin extraction close to zero. During twelve observation periods, in which the mean arterial blood pressure varied from 30 to 67 mm. mercury, renal blood-flow (in ml./gm./min.) was measured by the free outflow method, and the arteriovenous oxygen difference (in μmol./ml.) was determined manometrically[3]. It can be seen from Fig. 1 that the arteriovenous difference for oxygen rose sharply as blood-flow fell to less than 1 ml./gm./min., causing relatively constant consumption of oxygen over a wide range of variation in the rate of perfusion. This value was 0·215 ml. oxygen/gm. kidney/min. or 1·0 μmol./gm./min. (*S.E.* of mean, 0·04), and was considered to represent the basal oxygen uptake of the kidney. A basal oxygen consumption of a similar

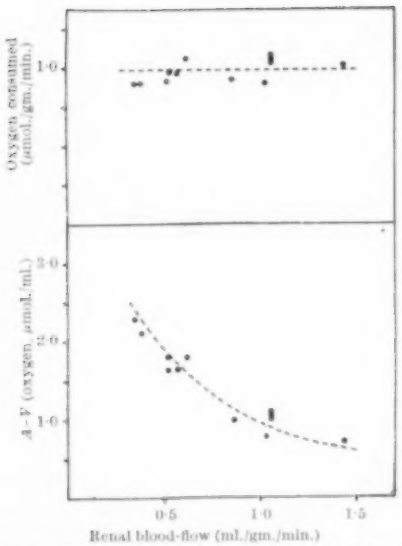

Fig. 1. Relationship between renal blood flow (in ml./gm./min.) and the arteriovenous oxygen difference (in μmol./ml.) of the non-filtering kidney during haemorrhagic hypotension. The calculated oxygen consumption has a mean value of 1 μmol./gm. kidney/min. and is seen to remain relatively independent of wide variations in the rate of blood perfusion

magnitude has been found in various exocrine glands of the dog: submaxillary[4] 1·4 and 1·2, parotid[5] 1·4, and pancreas[6] 1·3, μmol./gm./min.

The relationship between sodium re-absorption and suprabasal (net) oxygen consumption of the normally filtering kidney was determined on eight anæsthetized dogs. The femoral artery, the left renal vein and both ureters were cannulated, and standard clearance techniques were used involving inulin and sodium *p*-aminohippurate. Sodium re-absorption (in μequiv./gm. kidney/min.) was calculated from the amount filtered minus the amount excreted in the urine. The net consumption of renal oxygen (in μmol./gm. kidney/min.) was calculated as the product of the arteriovenous difference for oxygen and renal blood-flow, subtracting the basal oxygen consumption of 1·0 μmol./gm./min. The results are shown in Table 1. Despite large variations in the rate of sodium re-absorption, the sodium/net oxygen ratios remained fairly constant in the eight dogs. The mean ratio was 28·5 (*S.D.* 2·9) and is in agreement with the value of about 30 which can be estimated from data in the literature on normal man.

Table 1. Renal Oxygen Consumption and Sodium Re-absorption of the Dog

Dog No.	No. of observations	Sodium re-absorption (μequiv./gm./min.)	Total oxygen consumption (μmol./gm./min.)	Net oxygen consumption (μmol./gm./min.)	Sodium/net oxygen ratio
8	4	91·3	4·0	3·0	30
12	7	172·5	6·9	5·9	29
13	3	192·1	8·6	7·6	25
15	6	113·5	5·2	4·2	27
16	6	126·0	5·9	4·9	26
17	5	122·4	5·5	4·5	27
V	3	100·6	3·9	2·9	35
VII	3	103·1	4·6	3·6	29
Average		127·7	5·6	4·6	28·5 (*S.D.* 2·9)

The present results thus suggest that the intact mammalian kidney, like the isolated frog skin, has a fixed relation between sodium transport and net oxygen consumption. The sodium/net oxygen ratio has a somewhat larger value in the kidney (about 29) than in frog skin (about 18), but it is of interest that the consumption of one equivalent of oxygen (1/4 mole of oxygen) generates sufficient energy for the transport of several equivalents of sodium in both systems.

The concept that the renal oxygen uptake can be divided into a relatively small but constant basal uptake and a variable functional uptake, which is dominated by, and bears a constant relationship to, tubular sodium re-absorption, may explain some classical observations in renal physiology.

A large arteriovenous oxygen difference has been found in uncompensated heart disease, where the filtration fraction is large and the renal blood-flow reduced[7]. Conversely, a small arteriovenous oxygen difference results from infusion of albumin, which causes a reduction of the filtration fraction and an increase in blood-flow[8]. It is evident from the present hypothesis that variations in the filtration fraction may influence the arteriovenous oxygen difference; but it is important to consider also variations in renal blood-flow, since the basal oxygen consumption of the kidney must influence the arteriovenous oxygen difference the more the lower the rate of perfusion. Theoretically, variations in the arteriovenous oxygen difference $(A\text{–}V)O_2$, can be predicted if the following variables are determined: renal blood-flow (*RBF*), hæmatocrit (*H*), filtration fraction (*FF*), plasma sodium (P_{Na}), excretion fraction of sodium (E_{Na}), and renal weight (*W*):

$$(A\text{–}V)O_2 \text{ in ml./100 ml.} =$$

$$2{\cdot}24\left[W/RBF + \frac{1}{29}(1-H)(1-E_{Na})P_{Na}FF\right]$$

In contrast with other organs, a moderate reduction of renal blood-flow results in a decrease in renal uptake of oxygen. Since the filtration and hence re-absorption of sodium is also reduced in this situation, the observed correlation is readily explained. Only when blood pressure is reduced below the limit where filtration ceases, the kidney—like any other organ—extracts more oxygen per millilitre of blood in response to a reduction of the rate of perfusion, maintaining constant consumption of oxygen.

Thus, in both situations the kidney conforms to the general physiological principle first formulated by Barcroft[4], that oxygen consumption is directly related to function. Hence the seemingly puzzling difference between the oxidative metabolism of the kidney and other organs becomes merely a consequence of the unique fact that renal work is determined by, and roughly correlated to, renal blood-flow.

Renal oxygen consumption is not correlated to tubular *para*-aminohippurate transport or to urinary urea excretion[9]. These observations fit well into the theory of the dominant role of sodium transport, since no gross changes in the re-absorption of sodium occurred during the experiments, in which the effect of variations in renal handling of these two substances were studied.

The efficiency of the kidney is approximately 1 per cent when thermodynamic considerations are applied to the composition of the urine relative to plasma[10].

Such calculations disregard the oxygen cost of isotonic re-absorption of sodium. If renal oxygen

uptake is stoichiometrically related to the quantity of sodium re-absorbed, then the oxygen uptake cannot be expected to bear a fixed relation to the thermodynamically calculated (minimal) work involved in producing the final urine. Hence the concept of 'renal efficiency' may be considered physiologically meaningless.

This discussion has directed attention to some of the implications of applying the concept of a fixed sodium/not oxygen ratio to the mammalian kidney. More experiments are clearly needed in order further to investigate the validity and possible limitations of this concept.

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[1] Zerahn, K., *Nature*, **177**, 937 (1956); *Acta Physiol. Scand.*, **36**, 309 (1956).
[2] Leaf, A., and Renshaw, A., *Nature*, **178**, 156 (1957).
[3] Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, **61**, 523 (1924).
[4] Barcroft, J., *The Respiratory Function of the Blood* (Cambridge, 1914). Terroux, K. G., Sekelj, P., and Burgen, A. S. V., *Canad. J. Biochem. Physiol.*, **37**, 5 (1958).
[5] Ohara, K., *Jap. J. Physiol.*, **2**, 11 (1951).
[6] Still, E. U., Bennett, A. L., and Scott, V. B., *Amer. J. Physiol.*, **106**, 509 (1933).
[7] Merrill, A. J., *J. Clin. Invest.*, **25**, 389 (1946).
[8] Barker, H. G., Clark, J. K., Crosley, jun., A. P., and Cummins, A. J., *Amer. J. Med. Sci.*, **218**, 715 (1949).
[9] Clark, J. K., and Barker, H. G., *J. Clin. Invest.*, **30**, 745 (1951). Bucht, H., Werkö, L., and Josephson, B., *Scand. J. Clin. and Lab. Invest.*, **1**, 277 (1949). Van Slyke, D. D., Rhoads, C. P., Hiller, A., and Alving, A. S., *Amer. J. Physiol.*, **109**, 336 (1934).
[10] Rhoter, L. v., *Pflüg. Arch. ges. Physiol.*, **109**, 375 (1905).

Demonstration of Nucleases on Mammalian Skin Surface and in Saline Extracts of Hair

In the course of experiments on the effects of β-irradiation on the nucleases of guinea pig epidermis we washed thin strips of peeled tissue (25–60 μ thick) before homogenization, in an attempt to demonstrate release of enzyme[1]. Approximately 50 per cent of total deoxyribonuclease (DNase) and 75 per cent of ribonuclease (RNase) activity were thus removed from normal or irradiated epidermis, indicating that considerable amounts of these enzymes may be in the stratum corneum or in the interstitial fluid. This led us to test for the presence of enzymes on the closely clipped skin surface of living animals. For this purpose we adapted the plastic cup technique used by Peiss *et al.*[2] and Szakall[3] for the study of water and ion exchange between a chemically defined medium and the skin. Albino guinea pigs of either sex (500–900 gm.) were fed a vitamin C-enriched diet, anæsthetized with veterinary 'Nembutal' and clipped with an electric shaver. Plastic cups were secured to appropriate areas of the animals' flanks by means of ½ in. 'Trimtex' rayon elastic, and small alligator clamps or paper clips were used to fasten the elastic (No. *S*-2 plastic stoppers were supplied by Pioneer Plastics, Box 8066, Arlington Branch, Jacksonville 11, Fla.). Two small needle holes were punched 180° apart and about 6 mm. from the closed end of each cup; 1·5 ml. of 0·9 per cent saline was injected with a No. 22 needle and syringe, and samples were withdrawn for enzyme assay.

DNase activity was determined by the method of Schuster[4]. Assay solutions contained 1 mgm. of calf thymus DNA (Worthington) or salmon sperm DNA (California Foundation). Blanks were subtracted for enzyme added at zero time and substrate after 30 min. at 37° C. The increases in 260 mμ readings (Δ260) were proportional to DNase and RNase concentrations up to 0·2 *O.D.* RNase was determined by the method of Dickman *et al.*[5]; some of its characteristics have been described[6]. Saline in contact with normal epidermis was found to have considerable nuclease activity (Table 1). Since there was no increase in the nuclease content of these saline washings after 45 min. contact with the skin surface, this interval was chosen for sampling.

Table 1 Nuclease Activity of Saline Washings derived from 2·54 cm.² Normal Skin Surface and from Clipped Hair*

Animals	Sex	DNase Δ260/ml.			RNase Δ260/ml.		
		Initial sample	After 48 hr.	After 72 hr.	Initial sample	After 48 hr.	After 72 hr.
Guinea pigs	F	1·10	1·53	1·50	0·40	0·40	0·40
	F	0·90	1·40	1·40	0·05	0·25	0·25
	F	0·40	1·00	1·30	0·30	0·30	0·30
	M†	0·13	0·70	0·90	—	—	—
Albino rat	F	0·11	0·25	—	0·10	0·02	—
Albino rabbit	F	0·15	0·06	—	0·16	0·15	—
Guinea pig hair	F	—	1·50	—	—	0·70	—
Rat hair	F	—	0·4	—	—	0·47	—
Rabbit hair	F	—	0·25	—	—	0·70	—

DNase assay: 1 mgm. DNA, 0·1 *M tris* *p*H 7·4, 0·005 *M* magnesium sulphate and 0·1 ml. enzyme in 0·8 ml. final volume, 30 min. at 37°. Δ260 × 2 equals γ-crystalline DNase. RNase assay: 1·3 Michaelis (ref. 13) veronal-acetate buffer, *p*H 7·7; 0·2 ml. enzyme and 0·5 ml. 1 per cent dialysed yeast RNA, 15 min. at 37°. Δ260 × 0·1 equals γ-crystalline RNase.
* 1·5 gm. hair extracted in 10 ml. 0·9 per cent saline, for 48 hr. at 4° C.; 0·1 ml. aliquots for assay.
† Pigmented guinea pig.

The average enzyme activity of 1 ml. washings (4 animals) was equivalent to about 2 and 0·03γ of crystalline pancreatic DNase and RNase (Worthington), respectively (Table 1). Washing or wiping the skin surface prior to sampling removed most of it. About 24 hr. were required for surface nucleases to return to their initial level. In some instances, when the initial activity was low it rose to a high level after the second or third sampling of the area, 48 or 72 hr. later (Table 1). We have no explanation for this increase of enzyme after repeated sampling. Clipping the hair without touching the skin surface, in order to avoid trauma, results in levels comparable with closer clipping. The nucleases appear to be fairly uniformly distributed on the skin surface of the flanks. Nuclease activity can be leached out of the clipped hair (Table 1), but equally high levels are present on the depilated skin surface (Tabachnick, J., and Freed, R. M., unpublished results). Since there was no significant change in activity of the supernatant after centrifugation for 1 hr. at 100,000*g*, these enzymes are considered to be in solution in the saline washings and not associated with any cell particulate.

Skin surface DNase was inactive in the absence of magnesium ions. The optimal ionic strength (*p*H 7·0, Michaelis[13] veronal-acetate buffer), was about 0·17 in a complete medium to which sodium chloride had been added in varying concentrations. Heating the saline washings for 10 min. at 60° C. in a *p*H 4 or *p*H 7·4 buffer solution resulted in 90 per cent and 80 per cent losses of activity, respectively. As further evidence of enzymic hydrolysis of DNA we observed a

change in viscosity of a 0·1 per cent substrate solution from a gel-like consistency to a watery one within minutes after addition of an aliquot of active saline solution. In addition, paper chromatograms (70 per cent *iso*propanol-ammonia) of aliquots of DNA solutions, incubated 24 hr. with saline washings or crystalline DNase, showed similar broad bands of ultra-violet absorbing oligonucleotides which had left the origin. In controls, the ultra-violet absorbing material did not leave the origin.

The *p*H activity curve of skin surface DNase is similar to that of crystalline pancreatic DNase (DNase I), the optimum being at about 7·0 with little or no activity at or below 5·3. This indicates absence of an acid DNase (DNase II) which is present in many tissues[7]. Epidermis, washed free of extracellular enzyme prior to homogenization, contains DNase with a similar *p*H optimum, suggesting that the skin surface enzyme may be of epidermal origin. Unlike DNase I of liver or kidney, which may be masked by a specific inhibitor[7], the relatively high DNase activity at neutral *p*H on the skin surface or in guinea pig epidermis points to the absence of an inhibitor. Whether an activator[8] for DNase I is present remains to be determined.

In two human subjects (the authors) no nuclease activity was detected on the normal or sweating surface of the forearm, the palm, the nape of the neck, or in saline extracts of hair. The presence of non-specific esterases on human skin has been demonstrated with histochemical methods[9]. While skin bacteria play a part in the production of free fatty acids, some of the lipolytic activity was attributed to esterases of animal origin[10]. We found no significant changes in the amount of nuclease after reducing the bacterial count of guinea pig skin surface to 0 or 5 per cent by topical application of the antibiotics, 'Surgamycin' or 'Achrosurgic' (kindly supplied by the Lederle Laboratories Division, American Cyanamid Co., Pearl River, New York).

Steigleder[11] has referred to human skin surface as covered with an "esterase mantle", and regards human sebum and sweat as the chief carriers of the non-specific esterases. The present report suggests that other mammals, such as guinea pigs, have a nuclease coating. Since this species has no eccrine sweat glands, surface nucleases cannot originate there. In addition, in healed, β-irradiated guinea pig skin in which the dermal adnexal structures had atrophied or had been completely destroyed[12], we observed increases in surface DNase and RNase (Tabachnick, J., and Freed, R. M., unpublished results). Hence, in this animal, surface nuclease activity is probably of epidermal and/or humoral origin.

As shown in Table 1, rat and rabbit skin may also function as an excretory organ for nucleases. The question arises, Is there a selective removal of blood nucleases through the cutaneous blood vessels or are these enzymes a natural product of epidermal cell turnover and keratinization? This technique, applied to the surface of healed, irradiated skin with atrophied or destroyed adnexal structures, may prove to be a useful tool for obtaining answers to this and other questions relating to the *in vivo* permeability of the epidermis.

We are indebted to Dr. Peter Flesch, Department of Dermatology, University of Pennsylvania, Philadelphia, for directing our attention to the plastic cup technique[2,3]. A detailed report is in preparation. The work was supported by Contract *AT* (30-1)-1727 with the U.S. Atomic Energy Commission.

Note added in proof. The low levels of nuclease activity in the initial samples (column 3, Table 1) are the result of sampling immediately after close clipping of the animal's hair. Through the generosity of Prof. P. C. Trexler, Lobund Department of Biology, Notre Dame University, we recently had the opportunity of assaying saline extracts of germ-free hair obtained from guinea pigs, rats, and rabbits, and found levels of DNase and RNase activity as high or higher than the values in Table 1.

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[1] Tabachnick, J., Freed, R. M., and Weiss, C., *Rad. Res.*, **12**, 478 (1960).
[2] Peiss, C. N., Randall, W. C., and Hertzman, A. B., *J. Invest. Dermat.*, **26**, 459 (1956).
[3] Szakall, A., *Berufsdermatosen*, **6**, 171 (1958).
[4] Schuster, L., *J. Biol. Chem.*, **229**, 289 (1957).
[5] Dickman, S. R., Aroskar, J. P., and Kropf, R. B., *Biochim. Biophys. Acta*, **21**, 539 (1956).
[6] Tabachnick, J., and Freed, R. M., *Fed. Proc.*, **19**, 51 (1960).
[7] Feinstein, R. N., and Hagen, U., *Fed. Proc.*, **18**, 225 (1959).
[8] Feinstein, R. N., *J. Biol. Chem.*, **235**, 733 (1960).
[9] Steigleder, G. K., and Elschner, H., *Arch. klin. exp. Dermatol.*, **208**, 489 (1959).
[10] Scheimann, L. G., Knox, G., Sher, D., and Rothman, S., *J. Invest. Dermat.*, **34**, 171 (1960).
[11] Steigleder, G. K., *J. Invest. Dermat.*, **31**, 29 (1958).
[12] Tabachnick, J., and Weiss, C., *Rad. Res.*, **11**, 684 (1959).
[13] Michaelis, L., *Biochem. Z.*, **234**, 139 (1931).

Transplacental Passage of Red Cells in Man

The purpose of this communication is to report the results of an investigation into the frequency and magnitude of haemorrhage from the foetal to the maternal circulation in a random series of deliveries. The total separation of the maternal and foetal circulations was a long-held biological belief, and was only first seriously questioned in 1941, when the mechanism of haemolytic disease of the newborn was elucidated and Levine[1] showed that Rh iso-immunization occurred less often than expected in ABO incompatible matings. Because of these Rh findings, it was postulated that the antigen was carried across the placenta into the maternal circulation by intact erythrocytes.

Several investigators have since succeeded in demonstrating the passage of cellular elements across the placenta: radioactive tagged red cells, elliptocytes and sickle cells have been injected into the maternal circulation prior to delivery, and later recovered from the foetal circulation[2,3]. Foetal red cells have been detected in the maternal circulation by means of differential agglutination by Chown[4] and by Zipursky *et al.*[5], using the histochemical technique developed by Kleihauer *et al.*[6].

The technique used in the present work was that of Kleihauer, with the modification that the final preparation was unstained. The principle of the method is to elute haemoglobin A from the adult red cells by means of a citric-phosphate buffer; haemoglobin F remains in any foetal red cells and these stand out as dark refractile bodies (see Fig. 1).

To establish the sensitivity of the technique, 50 male bloods were examined along with 50 specimens of blood from post-partum women, the observer being unaware of the source of the specimens. Each specimen was given a quantitative score, this being the average of the number of refractile cells counted in four 3-min. scans. No male score exceeded 0·5.

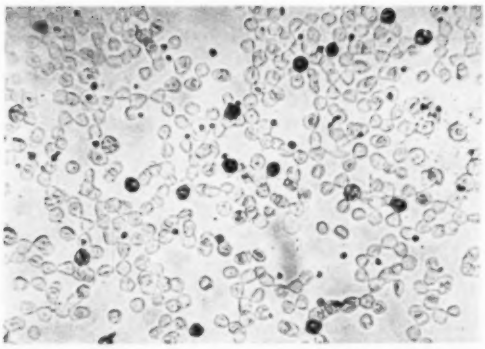

Fig. 1. Maternal blood from case of severe fœtal anæmia (hæmoglobin, 73 per cent) due to massive transplacental hæmorrhage. The fœtal red cells stand out darkly compared with the pale ghosted adult cells

Artificial mixtures of maternal and fœtal blood were next made at varying dilutions for the purpose of correlating the scores with actual amounts of fœtal blood. At a dilution of 1 : 5,000, the score was 5 (*S.D.* ± 1·5). Assuming an average maternal blood volume of 5 litres, this would represent 1 ml. of fœtal blood in the maternal circulation.

200 specimens of maternal blood were examined within 72 hr. of delivery. The average of two 3-min. counts was recorded, and scores of 2 or more were regarded as indicating definite transplacental hæmorrhage. This was detected in 12 per cent (24) of the women (Table 1).

Table 1. Fœtal Red Cells in 200 Specimens of Post-partum Maternal Blood. Scores recorded as Whole Numbers; for example, 2·5 is scored as 2

Fœtal red cells score	No. of specimens of post-partum blood	Fœtal red cells score	No. of specimens of post-partum blood
0	159	6	3
1	17	7	0
2	3	8	1
3	5	9	0
4	5	10–19	3
5	1	20–29	3

Scores of 10 or more were recorded on only six occasions (3 per cent), and this suggests that fœtal bleeding is rarely more than 1–2 ml. Work is in progress to find out the precise amount that is necessary to stimulate the formation of antibodies.

Though the amount noted in this random series was always less than 5 ml., we have investigated a case of marked neonatal anæmia (hæmoglobin 73 per cent) in which it was calculated that about 100 ml. of fœtal blood had entered the maternal circulation (see Fig. 1). It was shown afterwards that the mother was blood group S-negative and the fœtus S-positive, and *in vitro* it was clearly demonstrated that, on adding anti-S to the maternal blood, differential agglutination was produced (Fig. 2).

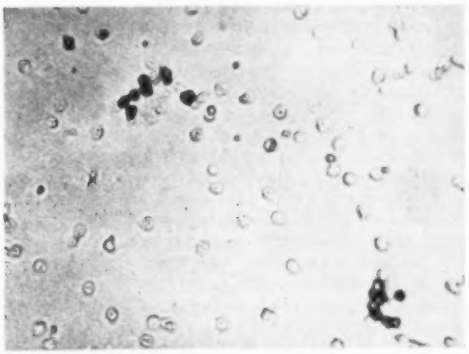

Fig. 2. Differential agglutination with anti-*S* at + 4° C. The small agglutinates stand out darkly (due to hæmoglobin F), thus confirming their origin from fœtal red cells

The results of the investigation have obvious relevance to the low incidence of iso-immunization in Rh-negative mothers as in the majority of cases the placenta seems to be an effective barrier against the entry of more than 1 ml. of fœtal blood. In Rh-negative patients in whom significant fœtal bleeding is detected immediately after delivery, it may be possible (as judged by the *in vitro* results) to inactivate the circulating fœtal cells by the administration of anti-D and thus prevent iso-immunization.

Using Rh-negative male volunteers, we have already shown that the administration of Rh-positive cells followed half an hour later by anti-D, results in these cells being coated with the antibody. In view of the results of Stern and Berger[7], it is hoped that this coating will prevent Rh-sensitization.

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[1] Levine, P., *J. Hered.*, **34**, 71 (1943).
[2] Naeslund, J., and Nylin, G., *Acta Med. Scand.* (Supp.), **170**, 126 (1946).
[3] Mengert, W. F., Rights, C. S., Bates, C. R., Reid, A. F., Wolf, G. R., and Nabors, G. C., *Amer. J. Obst. and Gynec.*, **69**, 678 (1955).
[4] Chown, B., *Lancet*, i, 1213 (1954).
[5] Zipursky, A., Hull, A., White, F. D., and Israels, L. G., *Lancet*, i, 451 (1959).
[6] Kleihauer, E., Hildegard, B., and Betke, K., *Klin. Wsch.*, **35**, 637 (1957).
[7] Stern, Kurt, and Berger, M., *Abst. from Thirteenth American Association of Blood Banks Programme*, 39 (1960).

RADIOBIOLOGY

Proliferative Cycle in the Growing Hair Follicle of the Mouse

The intermitotic phase has been divided into three segments: the phase of synthesis of deoxyribonucleic acid (DNA) (*S* phase), preceded and followed by 'gaps' called G_1 and G_2, respectively[1]. The duration of these phases can be accurately measured by pulse-labelling with tritiated thymidine, followed by serial killing, preparation of autoradiographs, and determination of the fraction of mitoses labelled at various intervals between injection and death[2,3]. Several kinds of cells have been so studied; the present communication adds to the list the cells of the growing-hair follicle in the mouse.

Young adult male *CF1* mice were used. Hair growth was initiated by plucking[4]. Tritiated thymidine (20 μc., sp. act. 1·9 c./m*M*) was administered

intraperitoneally 10–11 days after plucking, at which time hair growth is proceeding at full speed. Animals were killed at times ranging from 10 min. to 42 hr. after labelling. Autoradiographs were prepared; 50–100 ana- and meta-phases on each slide were scored for presence or absence of label. Presence of label indicates that the cell was synthesizing DNA during the period when label was available, that is, the first few minutes following injection[5]. When the interval between injection and death is short, no meta- or ana-phases are found to be labelled, because cells in this stage at the time of death were in G_2 or prophase at the time of labelling. Longer intervals yield labelled mitoses, since the cells in mitosis at the time of death were in S phase at the time of injection. Still longer intervals again result in unlabelled mitoses, since the injection in these cases coincides with the G_1 phase, mitosis, or G_2 phase of the preceding cycle.

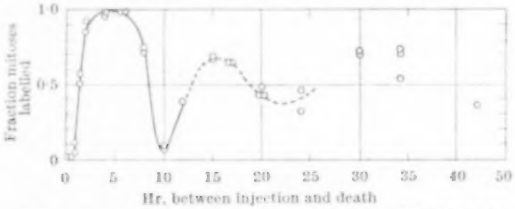

Fig. 1. Fraction of mitoses labelled as a function of the interval between injection of label and death. Each symbol represents one mouse

The results are shown in Fig. 1. The mean duration of the G_2 plus prophase is the interval between the origin and the time when 50 per cent of all meta- and ana-phases are labelled; it is 1·5 hr. The mean duration of the S phase is the width of the wave of labelled mitoses, measured between the two 50 per cent points; it is about 7 hr. The variability in the duration of the S phase can be estimated from the difference between the slopes of the ascending and descending limbs of the wave[3]; the standard deviation is about 0·9 hr. The distance between corresponding points on the first and second waves represents the generation time. However, since the second wave is not well defined, the estimation is equivocal; roughly, the generation time must be near 12 hr. Of this time, 8·5 hr. are taken up by the S and G_2 phases and prophase; allowing about 0·5 hr. for meta- and ana-phase, the remaining 3 hr. represent the mean duration of G_1. The distribution of durations of G_1 in individual cells can be roughly estimated from the shape of the second wave[3]. The data are compatible with an exponential distribution, possibly with some lag; this would imply that soon after the cells enter the G_1 phase there is a constant probability (of about 0·0055 min.$^{-1}$) that DNA synthesis will commence during the following minute.

The results of this work, together with findings in other cell systems, support a general impression that the duration of the S–G_2-mitosis sequence is fairly constant in a given species, while the duration of the G_1 phase varies widely and is chiefly responsible for differences in generation times, both within and between cell populations.

The amount of label in hair follicle cells is much less than in intestinal epithelial cells of the same animals. Maturing cells carry their label into the hair shaft, where it disappears at the same time as the nuclei. An artefact often seen is deposition of a dense layer of silver grains on the surface of hair.

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[1] Lajtha, L. G., *Physiol. Rev.*, **37**, 50 (1957).
[2] Quastler, H., and Sherman, F. G., *Exp. Cell Res.*, **17**, 420 (1959).
[3] Wimber, D. R., *Amer. J. Bot.*, **47**, 828 (1960).
[4] Chase, H. B., Rauch, H., and Smith, V. W., *Physiol. Zool.*, **24**, 1 (1951).
[5] Hughes, W. L., Bond, V. P., Brecher, G., Cronkite, E. P., Painter, R. B., Quastler, H., and Sherman, F. G., *Proc. U.S. Nat. Acad. Sci.*, **44**, 476 (1958).

Formation of an Ommatin Pigment from Tyrosine by Ultra-violet Irradiation

In the course of an investigation of the effect of ultra-violet irradiation on the formation of melanin from tyrosine, it was found that a brief period (5 min.) of irradiation had an effect similar to that brought about by the addition of a minute quantity of DOPA; on addition of tyrosinase to the irradiated solution oxygen uptake began immediately without an induction period, and ultimately reached a value approximating that calculated for conversion of the tyrosine to melanin. As the reaction proceeded, typical melanin granules were formed.

Attempts to bring about non-enzymatic melanin formation from tyrosine by irradiation were unsuccessful. Short periods of exposure to ultra-violet light resulted in the development of a golden-yellow product; limited increases in irradiation time had the effect of deepening the golden colour; but at no time was there evidence of melanin formation, even when solutions containing the yellow product were allowed to remain at room temperature for several days. Prolonged exposure to irradiation resulted in almost complete disappearance of this colour, with an accompanying drastic increase in oxygen uptake suggesting oxidative destruction. Changes in absorption spectra brought about by increasing dosages of irradiation indicated the formation of products having greater absorbency at 245–250 mμ and at 290–340 mμ than does unirradiated tyrosine. Analysis of solutions briefly exposed to ultra-violet radiation demonstrated the presence of DOPA quinone and of 5,6-dihydroxyindole.

The yellow pigment responsible for the change in absorbance was extracted by salting out with sodium chloride and shaking with *iso*butyl alcohol; the yellowish-tan muff formed at the interface was dissolved in alkali to give a reddish-brown solution. In Fig. 1, the spectra of the extracts indicate the formation of a product with maximum absorbance in the ultra-violet at 245 mμ, with a second peak at 300–305 mμ. That this product is not a melanin is shown by curve *D*, the absorption spectrum of a melanin obtained by enzyme action on briefly irradiated tyrosine. The pigment was insoluble in *iso*butyl alcohol until brought to *p*H 2; when it was extracted into alcohol at this *p*H, it exhibited a brilliant blue fluorescence with maximum emission in the region 410–430 mμ.

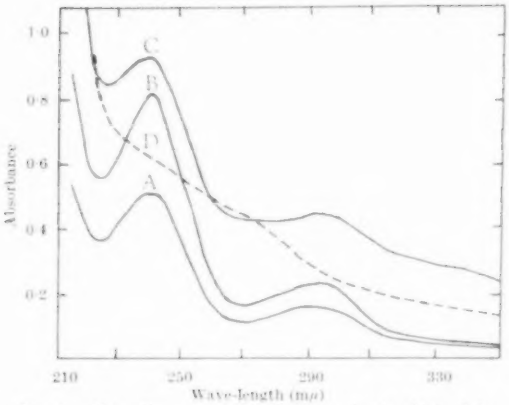

Fig. 1. Absorption spectra of pigment extracts obtained by irradiation of tyrosine for: *A*, 10; *B*, 20; *C*, 120 min.; *D*, purified melanin obtained by enzyme action on an irradiated tyrosine

In these characteristics, colour, relative insolubility, absorption spectrum in the ultra-violet region, and omission spectrum, the pigment, which is not an intermediate in the normal pathway of melanin formation, resembles the fluorescent red-yellow xanthommatin described by Butenandt *et al.*[1]. It is probable that as a result of irradiation, oxidation of the dihydroxyindole with the breaking of the 2 : 3 bond of the pyrrole ring has given rise to an *o*-amino phenol[2] which reacted with the DOPA quinone to form the ommatin pigment. This is of particular interest in relation to Fitzpatrick's[3] work on the production of pheomelanin, and as demonstrating an alternative pathway of pigment formation from tyrosine, one that is non-enzymatic.

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[1] Butenandt, A., Scheidt, U., Bickert, E., and Cromartie, R. J. T., *Ann.*, **590**, 75 (1954).

[2] Boyland, E., Sims, P., and Williams, D. C., *Biochem. J.*, **62**, 546 (1956).

[3] Fitzpatrick, T. B., and Kukita, A., *Pigment Cell Biology*, edit. by Gordon, M., 489 (Academic Press, New York, 1959).

HISTOCHEMISTRY

Enzyme Histochemistry of the Cells in Hodgkin's Disease and Allied Disorders

The complex nomenclature applied to cellular components of the reticuloendothelial system, based on their morphological characteristics, has resulted in a variety of controversial classifications of lympho-reticular neoplasia.

Enzyme histochemistry offers valuable assistance in identifying the various cell types and their malignant counterparts.

Braunstein, Freiman and Gall[1], in a preliminary report on the distribution of enzymatic activity in malignant lymphoma, stated that in general the enzymatic activity of cells of the various histiocytic types of malignant lymphoma corresponded to that of their normal counterparts. Of particular interest was the demonstration that the cells of reticulum cell sarcoma (histiocytic lymphoma) manifested enzyme activity identical with that of non-neoplastic histiocytes. They claimed also that large anaplastic cells and Sternberg cells of Hodgkin's 'granuloma' and sarcoma also manifested a similar pattern histochemically.

Methods for the histochemical demonstration of acid phosphatase, alkaline phosphatase and non-specific esterase[2] have been applied to lymph nodes and spleen in these laboratories, as part of a similar investigation.

The results of Braunstein *et al.* were confirmed, in part, in that histiocytes, wherever they were located, showed marked activity of acid phosphatase and non-specific esterase. Cells thought to be derived from histiocytes, for example, 'epithelioid' and 'endothelioid' cells and Langhans giant cells in tuberculous lymph nodes, together with foreign-body giant cells, reacted similarly. Splenic sinus lining cells, however, were consistently negative for these enzymes and are therefore not considered to be true histiocytes[3].

No reactions for these enzymes have been observed in lymphocytes. Alkaline phosphatase was confined to capillary endothelium, to some polymorphonuclear leucocytes and to an occasional mononuclear cell.

Twenty-seven cases of malignant lymphoma and leukæmia have been investigated. These included lymphocytic lymphoma (6), histiocytic lymphoma (reticulum cell sarcoma, 5), mixed lymphocytic-histiocytic lymphoma (1), follicular lymphoma (5), Hodgkin's 'granuloma' (6), Hodgkin's sarcoma (1), lymphocytic leukæmia (2), 'monocytic' leukæmia (1), and 'leukæmic reticuloendotheliosis' (1).

Strong non-specific esterase and acid phosphatase activity was observed in histiocytes (reticulum cells), however atypical and pleomorphic, in all these conditions. Moreover, these reactions demonstrated the abundant atypical histiocytes in five cases of follicular lymphoma, thus confirming the classification of Rappaport *et al.*[4], which includes, among others, mixed lympho-histiocytic and predominantly histiocytic types.

In Hodgkin's 'granuloma', however, mononuclear, binuclear (mirror-image) and multinuclear Reed–Sternberg cells were consistently negative for these enzymes, in striking contrast to the activity in adjacent reticulum cells. In one case of Hodgkin's sarcoma a minimal reaction for non-specific esterase was observed in some of the bizarre multinucleated cells.

No enzymatic activity was elicited from neoplastic lymphocytes.

The strong alkaline phosphatase of capillary endothelium demonstrated widespread proliferation of small blood vessels in all cases of Hodgkin's disease and around some foci of neoplastic tissue in other conditions. This feature is not obvious in routine paraffin sections, stained with hæmatoxylin and eosin.

In a case of 'monocytic' leukæmia, monocytoid cells infiltrating lymph nodes and spleen were also negative for these enzymes, in contrast to strong activity in surrounding histiocytes.

A case with long standing myelophthisic anæmia, followed by the occurrence of atypical mononuclear and multinuclear cells in the bone-marrow, monocytoid cells in the peripheral blood, lymphadenopathy, hepato-splenomegaly and widespread infiltration into the skin and subcutaneous tissues, was also encountered. This type of case has been designated 'leukæmic reticuloendotheliosis'. The monocytoid cells again showed no evidence of enzymatic activity.

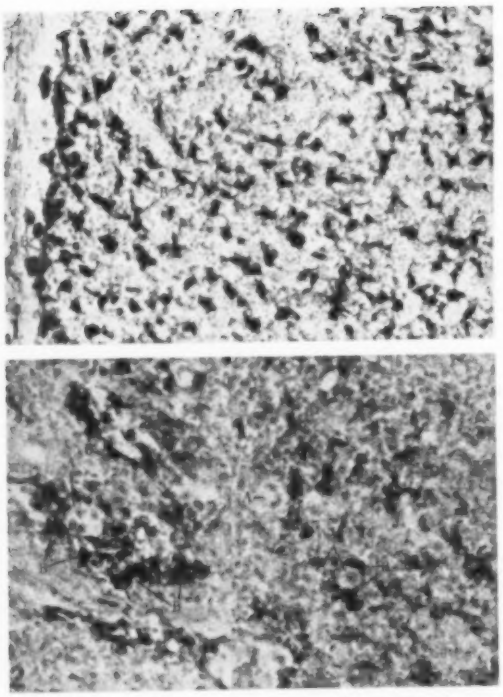

Fig. 1. Histiocytic lymphoma (reticulum cell sarcoma). Frozen section of a lymph node demonstrating non-specific esterase activity in malignant histiocytes (*B*); lymphocytes (*A*) show no activity. α-Naphthyl acetate method. (× *c.* 150)

Fig. 2. Hodgkin's disease. Composite photograph of frozen sections of lymph nodes showing non-specific esterase activity in histiocytes (*B*) but not in Reed–Sternberg cells (*A*). Mononuclear, binuclear and multinuclear cells are shown. α-Naphthyl acetate method. (× *c.* 150)

These findings indicate that, if Reed–Sternberg cells and monocytoid cells are derived from histiocytes (reticulum cells), then there has been a loss of activity of both non-specific esterase and acid phosphatase in the first two cell types. This seems most unlikely since there is no alteration in the reaction of these enzymes in malignant histiocytes. Furthermore, one would expect some cells to show a loss of activity of only one or other of the enzymes, especially in the less malignant form of Hodgkin's disease.

It seems probable, therefore, that both Reed–Sternberg and monocytoid cells are derived from cells other than histiocytes. That they may have a common origin from a primitive mesenchymal cell is not disputed, but, from the results of these enzyme studies, it appears that their relationship to the histiocyte is no closer than that of the lymphocyte to the histiocyte.

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1 Braunstein, H., Freiman, D. G., and Gall, A. E., *Amer. J. Path.*, **33**, 603 (1957) (abstr.).
2 Pearse, A. G. E., *Histochemistry: Theoretical and Applied*, second ed., 868 (Churchill, London, 1960).
3 Dorfman, R. F., *Nature* (in the press).
4 Rappaport, H., Winter, W. J., and Hicks, E. B., *Cancer*, **9**, 792 (1956).
5 Bouroncle, B. A., Wiseman, B. K., and Doan, C. A., *Blood*, **13**, 609 (1958).

Histochemical Analysis of some Dehydrogenase Systems in the Erythrocytes of some Lower Vertebrates

Recently I have studied histochemically three dehydrogenase systems, namely, succinic phosphopyridine nucleotide (DPN) and triphosphopyridine nucleotide (TPN) diaphorases and the DPN-dependent enzymes: lactic, malic, glutamic, β-hydroxybutyric, and ethanolic dehydrogenases, in the renal adenocarcinoma occurring in a laboratory strain of the oviparous toothcarp *Aplocheilus lineatus*[1]. In continuation of this investigation I decided to study the distribution of these enzymes, and also œstradiol-17β-dehydrogenase, in the erythrocytes of some of the lower vertebrates, namely, some teleosts, amphibians and reptilians.

These enzymes, with the exception of œstradiol-17β-dehydrogenase, were determined by the recently developed methods of Seligman, Nachlas and co-workers[2–5], based on the use of 2,2′-di-*p*-nitrophenyl-5,5′-diphenyl-3,3′-(3,3′-dimethoxy-4,4′-biphenylene)-ditetrazolium chloride (nitro-BT)[3] as the chromogenic electron acceptor. The sections were incubated at 37° C. for 15 min. Some sections were also processed with Regaud's stain[6] to demonstrate mitochondria. In general, for morphological orientation parallel sections were stained with haematoxylin and eosin, haematoxylin and azophloxin or thionin.

For incubation with the œstrogens, the erythrocytes were suspended in isotonic phosphate buffer, *p*H 7·4; and afterwards the suspensions were shaken at 20° C. For the comparative determinations of enzymatic activity, quantities containing the same haemoglobin content were used. Isolation, and qualitative and quantitative determination, of the steroids were carried out mainly by Repke's methods[7,8]. The œstradiol epimers were separated paper-chromatographically in the system chloroform–formamid.

The succinic dehydrogenase activity was low in the erythrocytes of all species investigated; it was linked to the cell membranes and the mitochondria. The DPN diaphorase activity appeared to be high, however. Also, this enzyme and the DPN-linked dehydrogenases were linked to the mitochondria and some cell membranes. The TPN diaphorase activity was much lower than the DPN diaphorase activity, and exhibited a widely dispersed and more finely intracytoplasmic distribution, which is certainly suggestive of the presence of microsomes and showed a high concentration in the cell membranes. The lactic dehydrogenase activity appeared to be rather high, the malic and β-hydroxybutyric dehydrogenase activities somewhat lower, whereas the glutamic and particularly the ethanolic dehydrogenase activity were generally low. The lactic dehydrogenase was more active than the malic dehydrogenase. As can be seen from Table 1, the enzymatic activities of the erythrocytes of the species investigated are mainly the same, although some minor differences can be established.

The œstradiol-17β-dehydrogenase occurred in the erythrocytes examined. This enzyme is capable of reducing œstrone to œstradiol-17β and of oxidizing œstradiol-17β to œstrone. An œstradiol-17β-dehydrogenase, found in ruminants, in addition to the œstradiol-17β-dehydrogenase[9], is not present in the erythrocytes of the lower vertebrates examined.

In general, the erythrocytes of the species examined correspond as regards œstradiol dehydrogenase

Table 1. Distribution of Succinic Dehydrogenase, DPN and TPN Diaphorase and Several DPN-Linked Dehydrogenases in the Erythrocytes of some Lower Vertebrates

The enzymatic activity was graded microscopically on the basis of colour reaction, 0 to 4, by inspection of the erythrocytes.

Enzymes	Teleosts										Amphibians							Reptiles					
	Anoitomus anadoma Linne	*Hemigrammus ocellifatus* Ahl	*Barbus tetrazona* (Bleeker)	*Betta macrocandha* (Bleeker)	*Aphyosemion coeruleum* (Boulenger)	*Xiphophorus helleri* Heckel	*Badis badis* (Hamilton)	*Aequidens pulcher* (Gill)	*Macropodus opercularis* (Linné)	*Brachygobius nunus* (Hamilton)	*Rana temporaria*	*Bufo calamita*	*Pipa pipa*	*Alytes obstetricans*	*Hyla arborea*	*Ambystoma mexicanum*	*Triturus cristatus*	*Salamandra salamandra*	*Lacerta agilis*	*Lygosoma spinosa*	*Anolis carolinensis*	*Testudo graeca*	*Agama agama*	*Varanus nilotica*
Succinic dehydrogenase	1	1	1	1	1	1	0	0	1	0	1	1	1	1	0	1	0	1	1	1	1	1	1	0
DPN diaphorase	4	4	4	4	4	4	3	3	4	3	4	4	4	3	3	4	3	3	3	3	3	3	4	4
TPN diaphorase	2	2	2	1	2	2	1	1	2	1	2	2	2	1	1	2	1	2	1	1	1	1	2	2
DPN-linked dehydrogenases																								
Lactic dehydrogenase	4	3	4	3	3	4	3	3	4	3	3	4	4	3	3	4	3	3	3	3	4	3	4	4
Malic dehydrogenase	2	2	2	2	2	2	1	1	2	1	2	2	1	1	1	2	1	1	1	2	1	1	2	2
Glutamic dehydrogenase	1	1	1	1	1	1	0	0	1	1	0	1	1	0	1	1	1	1	0	0	1	0	1	1
β-Hydroxybutyric dehydrogenase	2	1	2	1	2	2	1	2	1	1	2	2	2	1	1	2	1	2	1	1	1	2	2	2
Ethanolic dehydrogenase	1	0	0	0	0	1	0	0	1	0	0	1	1	0	0	1	0	0	0	0	1	0	1	0

activity with those in man, rabbit and guinea pig[9] and imperfectly with those in ruminants[10,11].

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[1] Stolk, A., *Proc. Kon. Ned. Akad. Wetensch., Amsterdam* (in the press).
[2] Seligman, A. M., and Rutenburg, A. M., *Science*, **113**, 317 (1951).
[3] Tsou, K. C., Cheng, C. S., Nachlas, M. M., and Seligman, A. M., *J. Amer. Chem. Soc.*, **78**, 6139 (1956).
[4] Nachlas, M. M., *et al.*, *J. Histochem.*, **5**, 420 (1957); *J. Biophys. Biochem. Cytol.*, **4**, 467, pl. 223 (1958); **29**, pl. 11 (1958).
[5] Monis, B., Nachlas, M. M., and Seligman, A. M., *Cancer*, **12**, 1238 (1959).
[6] Lillie, R. D., *Histopathologic Technic and Practical Histochemistry*, 183, second ed. (Blakiston Co., Inc., New York, 1954).
[7] Repke, K., *Arch. Exp. Path. Pharmakol.*, **230**, 178 (1957).
[8] Portius, H. J., and Repke, K., *Naturwiss.*, **47**, 43 (1960).
[9] Repke, K., and Markwardt, F., *Arch. Exp. Path. Pharmakol.*, **223**, 271 (1954).
[10] Levy, L. K., Hagopian, M., and Fish, C. A., cited by Dorfman, R. I., *Ann. Rev. Biochem.*, **26**, 547 (1957).
[11] Axelrod, L. R., and Werthessen, N. T., *Arch. Biochem. Biophys.*, **83**, 567 (1959).

Non-specific Esterase Activity in Histiocytes

Histiocytes in subcutaneous connective tissue are characterized by having marked phagocytic activity. We have reported previously that histiocytes increase their enzymatic activities in proportion to the degree of transformation of these cells under various irritations[1].

Recently, we have examined histochemically non-specific esterase activity in a dorsal subcutaneous spread from rabbits intensely stained with trypan blue. The dose of trypan blue was 10 c.c. of a 1 per cent solution injected intravenously once daily for seven days. It was found that histiocytes having trypan blue granules in their cytoplasm exhibited strong non-specific esterase reaction in discrete areas corresponding to the trypan blue granules. In contrast, fixed histiocytes, without phagocytosed particles, in a spread of normal subcutaneous tissue, showed strong diffuse enzymatic activity in their cytoplasm. It is not clear whether this non-specific esterase activity exists inside the trypan blue granules or around them. However, it is unquestionable that, when trypan blue is being ingested by the digestive vacuoles of the histiocyte and concentrated into granules within them, the non-specific esterase distributed in the protoplasm becomes organized and collects in the region of the trypan blue granules.

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[1] *J. Histochem. and Cytochem.*, **8**, 72 (1960).

PATHOLOGY

Evidence for Multiple Cæruloplasmin Components in Human Serum

More than one component of human cæruloplasmin has been reported by several investigators[1]. Morell and Scheinberg[1] have observed 4, possibly 5, components of cæruloplasmin by fractionating a pool composed of 9,109 individual sera. In such a large pool, infrequent unusual components would be easy to lose. Furthermore, the complex fractionation procedure provides opportunity for artefactual alteration of specific proteins. The resolving power of vertical starch-gel electrophoresis[2] combined with direct chemical and enzymic analysis on the gel provides a simple and elegant means of examining the problem in individual sera. Using this technique we have found 5 electrophoretically distinct proteins having one or more characteristic properties of cæruloplasmin.

Sera were obtained from 43 pregnant women (in the third trimester of pregnancy or within a few days *post partum*), 17 patients with various diseases (Table 1) and 5 normal individuals. A voltage gradient of 5 V./cm. was maintained for periods of 16–20 hr. at room temperature. Half of each starch-gel block was stained with amido black $10B^2$; the other half was stained with *p*-phenylenediamine dihydrochloride (PPD), employing a modification of the method of Morell and Scheinberg[1]. Filter paper strips were saturated with a 1·0 *M* acetate buffer (*p*H 5·0) which contained 0·5 per cent PPD. These strips were pressed on the cut surface of the block for 5 min. and

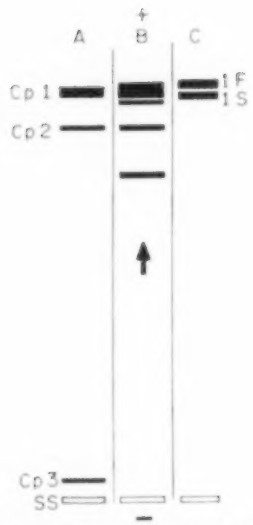

Fig. 1. Schematic diagram of the results of vertical starch-gel electrophoresis of serum of a pregnant human (*A*), cæruloplasmin concentrate, K.A.A.B.I. *DWZ* 71 (*B*) and 2 sera with atypical cæruloplasmins (*C*). *Cp* 1, Principal cæruloplasmin component; *Cp* 2 and *Cp* 3, probable and presumptive minor cæruloplasmin components respectively; 1*F*, major PPD oxidase component with fast mobility in serum of normal pregnant human; 1*S*, major PPD oxidase component with slow mobility in serum of patient with the muco-cutaneous syndrome

then removed. The block was allowed to stand at room temperature for the next 6 hr., during which time a deep purple colour developed in the region of the fast α-2-globulins. This principal component (*Cp* 1 of Table 1 and Fig. 1) was found in all specimens except one from a patient with Wilson's disease. Two other patients with this disorder had markedly diminished but detectable amounts of this material having a mobility exactly like that of the principal component of normal individuals. A principal component having a slightly faster mobility (*Cp* 1*F*) was found in the serum of one normal pregnant woman; one with a slightly slower mobility (*Cp* 1*S*) was found in the serum of a patient with the muco-cutaneous syndrome[3].

In the area associated with the transferrins, a second violet band of products of PPD oxidation (*Cp* 2) was found in specimens from all pregnant subjects, from one normal female, from a patient with carcinoma of the lung and from a patient with prostatic carcinoma who had been receiving stilbœstrol for 5 years. The second band in all cases was considerably less intense than the main component. A second examination was needed to demonstrate its presence in the sera of a few pregnant subjects.

A very faint third component (*Cp* 3) appeared immediately in front of the sample insertion slot in all sera for which it was examined (3 normal and 21 pregnant subjects).

A commercially prepared cæruloplasmin concentrate of human *post-partum* serum (lot *DWZ* 71 from K.A.A.B.I. of Stockholm) showed a very intensely stained principal component covering a broad zone in the fast α-2-region, apparently comparable to *Cp* 1 described above, and a second band with the same mobility as that of *Cp* 2 described above. Two much fainter bands were also found: one between the principal component and the second band and another with considerably slower electrophoretic mobility than the second band.

Several blocks were stained by filter paper strips saturated with 1·0 *M* acetate buffer (*p*H 5·0) which contained 6 m*M* concentrations of serotonin creatinine sulphate, L-adrenaline or L-nor-adrenaline bitartrate. These strips were pressed on the cut surfaces of the starch blocks and left there for 15 min. Coloured products developed during the next 24 hr. in the α-2-globulin region (*Cp* 1) of samples from normal and pregnant individuals and in the K.A.A.B.I. cæruloplasmin concentrate. Staining of *Cp* 2 in the region of the transferrins was visible only in the cæruloplasmin concentrate.

Blocks were stained for copper by placing them in a saturated ethanolic solution of rubeanic acid for 24 hr., after which time greenish-black bands were seen at the sites of *Cp* 1 and *Cp* 2. Visual estimates of the PPD staining intensity suggest that the concentration of *Cp* 3 is of the order of 1/1,000th that of *Cp* 1; its failure to react with rubeanic acid may therefore be due to its low concentration.

The *Cp* 1 component has the principal characteristic properties of cæruloplasmin: it has a natural blue colour, contains copper, and oxidizes PPD, 5-hydroxytryptamine, adrenaline and nor-adrenaline[4,5]. *Cp* 2 contains copper and is visibly capable of oxidizing PPD and the other substrates; this is probable evidence that this protein is a cæruloplasmin. *Cp* 3 oxidizes visibly PPD; this is presumptive evidence that this protein is a cæruloplasmin. *Cp* 1*F* and *Cp* 1*S* have not as yet been examined in detail with respect to properties other than PPD oxidation.

The occurrence of the *Cp* 2 in pregnant women and in a male receiving stilbœstrol suggests that œstrogens influence the appearance of this protein in detectable amounts. In all these cases, *Cp* 1 was visibly increased in concentration as compared with that found in normal sera; this is in accordance with the known ability of œstrogens to influence cæruloplasmin as measured by other techniques[4]. The appearance of *Cp* 2 appears to be determined by some factor other than concentration, since it could not be found in normal sera which had been concentrated five-fold and ten-fold, raising the concentration of the *Cp* 1 component to the equivalent or excess of that seen in the serum of pregnant subjects (serum was placed in a dialysis casing which was suspended in air in front of an electric fan).

Table 1

Group	No. of subjects	*Cp* 1	No. with *Cp* 2	*Cp* 3
Normal subjects	5	5	1	3
Pregnant subjects	43	43*	43	21
Subjects with disease states:				
Wilson's disease	3	2	0	—
Bronchogenic carcinoma	3	3	1	—
Huntington's chorea	2	2	0	—
Chronic bronchitis	1	1	0	—
Malignant lymphoma	1	1	0	—
Multiple myeloma	1	1	0	—
Prostatic carcinoma	1	1	1	—
Active tuberculosis	1	1	0	—
Schizophrenia	2	2	0	—
Personality disorder	1	1	0	—
Muco-cutaneous syndrome	1	1†	0	—
Total	65	64	46	24 (out of 24 studied)

* One specimen had atypical (fast) mobility.
† Atypical: (slow) mobility.

The atypical components, *Cp* 1*F* and *Cp* 1*S*, are being investigated further by means of family studies.

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Note added in proof: *Cp* 1*S* has a normal mobility when the haptoglobin (type 1-1) is completely removed from this zone by saturation with haemoglobin. Blood relatives of this patient all have the normal *Cp* 1. A study of four generations of the family in which *Cp* 1*F* is segregating indicates inheritance of the trait as a dominant character. *Cp* 1*F* is differentiated more readily from *Cp* 1 at *p*H 9·5 (0·0125 *M* borate buffer).

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[1] Morell, A. G., and Scheinberg, I. J. *Science*, **131**, 930 (1960).
[2] Smithies, O., *Biochem. J.*, **71**, 585 (1959).
[3] Bøe, J., Dalgaard, J. B., and Scott, D., *Amer. J. Med.*, **25**, 857 (1958).
[4] Laurell, C. B., in *The Plasma Proteins*, edit. by Putnam, F., **1**, 361 (Academic Press, New York and London, 1960).
[5] Martin, G. M., Benditt, E. P., and Eriksen, N., *Arch. Biochem. and Biophys.*, **90**, 208 (1960).

BIOLOGY

Effect of 5-Bromuracil on Crown Gall Tumour Induction

Crown gall tumours in plants are initiated by the action of virulent strains of *Agrobacterium tumefaciens* (Smith and Town) Conn on susceptible plant cells. Once these cells have been altered to tumour cells, the presence of the bacteria is no longer required for their continuing, autonomous growth[1]. The unknown agent or method by which this alteration of properly conditioned cells to tumour cells is accomplished is not known[2]. There have been a number of recent claims that this agent is a nucleic acid, specifically a deoxyribonucleic acid (DNA)[3,4] or that DNA plays some accessory part in tumour induction[5]. Some of these claims have been subject to critical examination and have been shown to rest on inadequate evidence[6].

The most recent claim that the transforming agent may be a DNA rests on the work of Bopp[4], who reported that the pyrimidine analogue 5-bromuracil does not inhibit the growth of *A. tumefaciens*, the wound-healing reaction of the host plant, or the growth of induced tumours, but does inhibit the initiation of tumours. This communication is concerned with an evaluation of these findings.

Four different samples of 5-bromuracil were obtained from commercial laboratories. Sample 1 was purchased from California Biochemicals, Los Angeles, California; sample 2 was purchased from Mann Research Laboratories, New York; sample 3 was a sample used by Dr. Bopp in his experiments and kindly sent to us; it was manufactured by Fluka A. G., Buchs, Switzerland; while sample 4 was purchased from Nutritional Biochemicals Corporation, Cleveland, Ohio.

The effect of these samples at a concentration of 200 μgm./ml. on the generation time of the bacteria is shown in Table 2. In these experiments the bacteria were grown in a defined medium[7] for 24 hr., then diluted 100,000 times into special flasks equipped with tubes for photometry. The medium containing 5-bromuracil and the control medium were both filter-sterilized through *HA* Millipore filters (Millipore Filter Corp., Bedford, Mass.), because it was found that autoclaving destroyed the inhibitory principle in sample 4. Not enough of sample 3 was available to test the effects of autoclaving on its growth-retarding component. The flasks were shaken about 150 times per minute on a motor-driven shaker in an incubator kept at 27° C. Turbidimetric readings were made with a Coleman, Jr., spectrophotometer at 410 mμ.

The effect of 5-bromuracil on tumour induction was tested by inoculating the midrib of young *Kalanchoe daigremontiana* (Hamet and Perrier) leaves with the highly virulent strain *B6* of *A. tumefaciens* and placing one drop of a solution containing 200 μgm./ml. 5 bromuracil on the inoculation site on the day of inoculation and on 3 successive days. Water was applied to the control inoculations. About two weeks later the infected sites were scored independently by each of us. The average for 32 inoculations is given in Table 1. These results clearly indicate that samples 1, 2, and 3 did not interfere with tumour induction, whereas sample 4 had a definite inhibitory effect.

Table 1. The Effect of 5-Bromuracil on Bacterial Growth and Tumour Induction

Treatment	Bacterial growth (in terms of generation time)	Average tumour score*
Control (water)	2·5	1·5
Sample 1, 200 μgm./ml.	2·5	1·6
Sample 2, 200 μgm./ml.	2·5	1·6
Sample 3, 200 μgm./ml.	3·0	1·6
Sample 4, 200 μgm./ml.	4·0	0·4

* Scoring: 0 = no reaction, 0·5 = questionable reaction, 1 = definite reaction, and 2 = strong reaction.

Chromatographic analysis of the four samples by ascending paper chromatography on Whatman No. 1 paper was carried out in two separate solvent systems. In an *n*-butanol/water (43 : 7) system, samples 1, 2, and 3 showed an ultra-violet absorbing spot at $R_F \sim 0{\cdot}35$; no other spots were detectable. In an *iso*-propanol/hydrochloride (13 : 7) system, samples 1, 2, and 3 showed ultra-violet absorption only at $R_F \sim 0{\cdot}60$; sample 2 had a slight 'tail' behind it. Sample 4 did not show any ultra-violet absorbing or other ultra-violet detectable spots at any point past the origin in either of these two solvent systems. Samples 1 and 2 were white, sample 3 was light pink, and sample 4 had a pinkish tinge. Elemental analysis of these samples was carried out by Mr. S. T. Bella of the Rockefeller Institute. The results of these analyses are shown in Table 2 and confirm the chromatographic evidence of the impurity of sample 4.

Table 2. Elemental Analysis of Four Samples of 5-Bromuracil

Sample	Carbon	Hydrogen	Nitrogen
1	25·18	1·64	15·38
2	25·41	1·45	14·89
3	25·50	1·51	*
4	16·39	1·75	15·43
Theoretical	25·14	1·58	14·67

* Insufficient sample available for nitrogen determination.

These results indicate that there is associated with certain commercially available samples of 5-bromuracil a heat-labile impurity which does not absorb in the ultra-violet. This impurity inhibits bacterial growth and thus cannot be considered a specific inhibitor of tumour induction. We suggest that the tumour inhibition observed by Bopp reflects the presence of an impurity in his samples. Such an impurity, although inhibitory to the bacteria, would not have been detected by means of the bacteriological techniques which he employed.

Samples of comparatively pure 5-bromuracil failed to inhibit tumour induction, thus seriously questioning the validity of the data which were interpreted to indicate that 5-bromuracil specifically inhibits the formation of an effective tumour-inducing agent and that such an agent might be a DNA.

We acknowledge the interest and support of Dr. Armin C. Braun during this investigation.

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[1] Braun, A. C., and White, P. R., *Phytopath.*, **33**, 85 (1943).
[2] Braun, A. C., and Stonier, T., *Protoplasmatol.*, **10** (5*a*), 1 (1958).
[3] Klein, R. M., and Knapp, J. L., jun., *Proc. U.S. Nat. Acad. Sci.*, **43**, 199 (1957).
[4] Bopp, M., *Planta*, **54**, 221 (1960).
[5] Manigault, P., and Stoll, C., *Experientia*, **14**, 409 (1958).
[6] Klein, R. M., and Braun, A. C., *Science*, **131**, 1612 (1960).
[7] Stonier, T., *J. Bacteriology*, **79**, 889 (1960).

Seasonal Acclimatization of Oxygen Consumption to Temperature in a Tropical Poikilotherm, the Earthworm, *Megascolex mauritii*

Seasonal acclimatization of oxygen consumption to temperature has been demonstrated in poikilotherms by many authors, and its profound ecological significance is widely recognized[1-5]. But most such investigations are restricted mainly to marine organisms of cold and temperate zones. Comparatively little attention has been paid to such seasonal compensatory changes in oxygen consumption in tropical, freshwater and amphibious animals and much less in the terrestrial forms. Except for the work of Vernberg[6] on intertidal crabs, nothing has been reported of the seasonal fluctuations of respiration in any tropical poikilotherm.

The results of this work show the existence of a homoiostatic mechanism in oxygen consumption, compensating for the seasonal temperature changes in the tropical earthworm, *Megascolex mauritii*.

The oxygen consumption of these worms was measured under water at 15°, 20°, 25°, 30°, 35° and 40° C., by Winkler's method[7]. The determinations were made during the winter (January) and the summer (June) of 1959 and 1960. Measurements at 40° C. in June 1959, and those at 15° C. in June 1960, could not be made. The results for the year 1960 are presented in Fig. 1. The regression lines for 1959 summer samples are also included for comparison.

Acclimatization of oxygen consumption to seasonal change in temperature occurs in the tropical earthworm *Megascolex mauritii*, as may be seen from the fact that, at all the temperatures investigated, the metabolism of the winter animals (lines *A* in Fig. 1) was higher than that of the summer samples (lines *B* and *C*). The difference in the slopes of the regression curves of winter and summer animals indicates that the effect of weight on oxygen consumption changes with season. In other words, the degree of acclimatization to temperature varies with weight. The degree of acclimatization may be greater in smaller worms, which generally consume oxygen at a higher rate than larger worms. This difference, between smaller and larger worms, in the degree of acclimatization to seasonal temperature changes, explains the flat and steep regression curves of oxygen consumption of winter and summer populations, respectively. Another fact that is clear from Fig. 1 is that the June 1959 population (lines *B*) utilized more oxygen than that of the June 1960 (lines *C*).

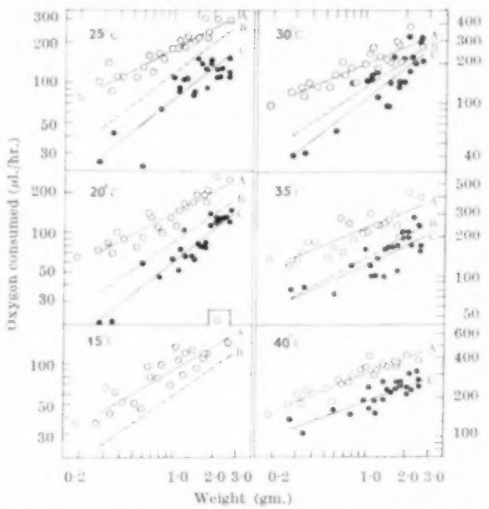

Fig. 1. Oxygen consumption in *Megascolex mauritii* as a function of size and temperature during winter and summer. Each point represents an individual measurement; double logarithmic grid; *A* (open circles), winter animals of January 1960; *B*, summer animals of June 1959; *C* (closed circles), summer animals of June 1960

Roberts[8], working on population samples of *Pachygrapsus crassipes*, could not detect any seasonal thermal acclimatization of respiration. Recently, it was shown by Vernberg[6] that no seasonal variation in oxygen consumption was to be found in the tropical form, *Uca rapax*, whereas a marked seasonal acclimatization was exhibited by the temperate form, *Uca pugnax*. This absence of seasonal acclimatization to temperature in the tropical crab, he thought, might be due to small annual temperature fluctuations. He also felt that the results of Roberts on *P. crassipes* might be due to low annual fluctuations in temperature. But the high and low mean monthly temperatures recorded by Roberts were about 12° C. in January and 22° C. in August. The high and low mean temperatures recorded during my investigation were 35° C. in May 1959, 36·5° C. in May 1960, and 25·5° C. in December 1959. Though the difference in the high and low temperatures is nearly the same in both cases, it is interesting to note that good metabolic acclimatization to seasonal change was observed in this tropical form.

The difference in oxygen consumption between the two summer populations of June 1959 (lines *B*) and June 1960 (lines *C*) can be correlated with the history of temperature during the two summer seasons (Table 1). The temperature during summer 1960 was not only higher (36·5° C.) than in 1959 (35° C.) but also was maintained for a longer duration. It is noteworthy that the degree of thermal acclimatization of oxygen consumption in summer populations depends on the intensity as well as the duration of high temperature during that particular season.

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Table 1. STATEMENT OF MEAN MONTHLY TEMPERATURE (IN °C.) DURING WINTER AND SUMMER OF 1959 AND 1960

Year	Winter		Summer			
	Dec.	Jan.	Mar.	April	May	June
1959	—	—	31·5	33·5	35	35
1960	25·5	26	31·5	35	36·5	36

Similar work, during the same period (January and June 1960), on another tropical earthworm, *Octochætus* sp., also showed a good seasonal acclimatization of respiration to temperature and this acclimatization was more evident in the smaller worms.

A complete report will be published elsewhere.

I wish to express my gratitude to Prof. Kandula Pampapathi-Rao, head of the Department of Zoology, Sri Venkateswara University, Tirupati, for his interest and guidance throughout. Part of this work was carried out during the tenure of a junior research fellowship of the Council of Scientific and Industrial Research, New Delhi.

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[1] Bullock, T. H., *Biol. Rev.*, **30**, 311 (1955).
[2] Prosser, C. L., *Biol. Rev.*, **30**, 229 (1955).
[3] Pampapathi-Rao, K., *Symp. Zool. Soc. India Bull.*, No. 3, 6 (1959).
[4] Berg, K., *Hydrobiologia*, **5**, 331 (1953).
[5] Vernberg, F. J., *Physiol. Zoöl.*, **25**, 243 (1952).
[6] Vernberg, F. J., *Biol. Bull.*, **117**, 163 (1959).
[7] Saroja, K., *Proc. Ind. Acad. Sci., Sect. B*, **49**, 183 (1959).
[8] Roberts, J. L., *Physiol. Zoöl.*, **30**, 242 (1957).

A Hermit Crab New to Britain

OF recent years the hermit crab *Clibanarius misanthropus* (Risso) has been reported from stations successively farther north along the coast of the Bay of Biscay[1]. It seems probable that this represents a true northerly advance of this example of an essentially tropical genus, for it is unlikely to have been overlooked since its almost exclusively intertidal habit and its brilliant colours attract the attention. By 1957 it had been reported to the north of Brest, but it does not seem yet to have been found along the north French coast; in particular, the collectors of the Station Biologique at Roscoff have not found it. Indeed, Crisp and Fischer-Piette[1] advance reasons for supposing that it is unlikely to spread along this coast. On the other hand, the drift of surface water which occurs in some years from Finistère towards Land's End or towards the Scilly Islands might be expected to carry larvæ to the British shores. Despite regular surveys of the shores of the Scilly Islands, our colleagues have not found this species there; but during the early months of 1960 large numbers were found on the shore at Mousehole on the southern coast of Cornwall (lat. 56° 6′ N., long. 5° 31′ W.), near Land's End. It is significant that the water at the western end of the English Channel in March and April 1959 (when the larvæ of *C. misanthropus* would be planktonic) had an unusually high salinity, suggesting the presence of Biscay water flowing into the Channel.

C. misanthropus is a hermit crab with subequal claws and hence quite unlike any of the native species which have unequal claws. It seems likely that it was not present on this shore before the winter of 1959–60, to judge by the reports of amateur collectors in this region, nor has it been found on any of a number of beaches and shores in the neighbourhood. During the winter it was the commonest hermit crab at about mid-tide level on this one shore, as many as 48 being found in one small rock-pool, together with no more than 2 specimens of other species; in the summer it has been confined mainly to pools lower down on the shore, around low-water neap tide mark, but is still abundant. Most of them inhabit shells of *Littorina* sp., while a few are in shells of *Nucella*. In this they contrast with the French specimens, which were mainly found in *Gibbula* or *Monodonta* shells. During the winter all the animals collected were of nearly the same size; but in September 1960 a number of much smaller crabs were present in the population, suggesting that they had bred successfully. It will be interesting to observe if they succeed in permanently colonizing British shores.

It has been suggested[1] that *Pagurus fasciatus* Bell is identical with this species. Bell[2] described and named *P. fasciatus*, without ever having seen a specimen, from a coloured drawing supplied by a Mr. Cocks of Falmouth, where, presumably, he collected his specimen. We feel that this identification cannot be correct, but the description is too vague for any certainty. There is just a slight possibility, therefore, that *Clibanarius misanthropus* has been taken before on the south coast of Cornwall, more than a hundred years ago.

We wish to thank Dr. A. F. Turk for his interest.

Note added in proof. During spring, 1961, a new year-class has appeared at Mousehole and specimens of this same (new) year class have been collected at Wembury, a similar habitat on the southern coast of Devon, 105 km. east of Mousehole. Since Wembury (lat. 50° 19′ N., long. 4° 5′ W.) is probably the commonest collecting ground of all for workers and students at the Plymouth Laboratory, it seems exceedingly unlikely that *Clibanarius* should have been present in earlier years. It thus seems that it is continuing its northward and westward spread.

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[1] Crisp, D. J., and Fischer-Piette, E., *Ann. Inst. oceanogr. Monaco*, **36**, 275 (1959).
[2] Bell, T., *A History of British Stalk-eyed Crustacea* (Ray Soc., London, 1853).

A Bathyal-abyssal Hermit Crab with a Calcified Asymmetrical Abdomen

IN the highly productive part of the Pacific Ocean, off Central America, the Danish *Galathea* Deep-Sea Expedition in 1952 made an exceptionally rich haul with a large herring otter trawl at a depth of 3,570 m. This haul yielded *inter alia* the first known species of *Neopilina* and a total of 126 species and about 2,100 specimens of benthic animals.

The 10 species of decapod crustaceans comprised 18 specimens of a pagurid, *Probebei mirabilis*[1]. This genus and species was described by Boone[2,3] as "a primitive macruran crustacean". First and foremost, because of the calcified abdomen the author did not recognize it as a pagurid, and apart from a reference to it in the *Zoological Record* of 1926 it has since been almost totally neglected, for example, in Bronn, by Melin[4], Gordan[5], and others. Within the Paguridea it belongs to the Pagurinae Latr. (= Eupagurinae Ortm.). Boone's family Probebeidae[3] is thus invalid.

The holotype was the only specimen collected by the *Arcturus* Expedition in 1925, south of Cocos Island in the Gulf of Panama at 1,145 m. depth. It belongs to the youngest post-larval stage which was represented in the *Galathea* material, and is 20 mm. long.

The largest of the adult specimens measures 65 mm. The carapace is somewhat broadened and furnished with many short spines and a long rostrum. The abdomen is moderately large, completely calcified dorsally, almost entirely symmetrical in the male and somewhat asymmetrical in the female, the left part of each segment being a little longer than the right and with only the left pleopods developed. The telson is symmetrical in both sexes. The right cheliped is slightly larger than the left, and peræopods II and III are very elongated as in *Tylaspis*, the hitherto deepest recorded hermit crab[6]. The male has the first pair of pleopods preserved, the female pleopods 2–5.

Phylogenetically the genus is most closely related to other genera with paired pleopods in the male and with a corresponding number of pairs of gills (eleven): *Parapagurus*, *Sympagurus*, *Tylaspis*, and *Tomopagurus*. Apart from the latter, which occurs at a depth of 132 m. off the Barbados, the remaining genera are bathyal or abyssal.

A number of instances are known of hermit crabs having evolved means other than a gastropod shell for protection of the abdomen, probably first and foremost because of lack of sufficient shell material. Primarily in the deep sea, several species have taken advantage of *Dentalium* shells, pieces of wood or bamboo, polychæte tubes, etc. In *Tylaspis*[6] and especially *Ostraconectes*[7], the abdomen has become reduced and is probably unprotected, although it is soft-skinned and can only, to a lesser degree, be folded under the cephalothorax. In these two genera, in practically all the species with an almost straight protective object, and in the three instances mentioned below, the animals have acquired a secondarily symmetrical or almost symmetrical abdomen; but their origin from asymmetrical forms in gastropod shells is always discernible by the presence of unpaired, left-hand pleopods, at any rate in the females. Furthest advanced along this line are those forms which have regained the calcified abdomen of their ancestors (the primitive, quite symmetrical Pylochelidae and the Thalassinidea), namely: (1) the stone crabs (Lithodidae); (2) the robber crab (*Birgus latro*); (3) *Probeebei*, which all originate from the Paguridae but which have evolved from systematically very differing stocks within the family[8]. The Lithodidae are fully 'carcinized'[9], with the comparatively small abdomen firmly pressed against the cephalothorax, with a very crab-like carapace, and with peræopods IV as long as II and III.

Birgus and *Probeebei* represent parallel lines of evolution in environments—dry land and abyssal depths—both of which are extremes in comparison with the warm shallow water in which the pagurids primarily evolved. In both cases the secondary calcification of the abdomen must be due to lack of sufficient shell material. The calcification is further advanced in *Probeebei*; but in several other respects the evolution to a freely roaming animal has caused a considerably greater change of the adult *Birgus* than of *Probeebei*: peræopod IV is comparatively much larger and can be used for walking; not only the male but also the female abdomen are practically symmetrical (apart from the lack of right pleopods), and the uropods have become almost completely reduced; also in the adaptation to the life on dry land (shape of eye-stalks, antennulæ and antennæ, presence of lungs, behaviour, etc.[10]), *Birgus* is much more advanced than the species of the closely related genus *Coenobita*, which are likewise land-dwelling.

On most islands where *Birgus* occurs it outgrows the available land snails soon after having left the sea, but the metamorphosis into the free-living stage can be considerably postponed experimentally[11]. It is to be hoped that future investigations in the area of distribution of *Probeebei mirabilis* will reveal the early post-larval development of this species, which may prove as interesting as that of *Birgus latro*.

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[1] Wolff, T., *Galathea Rep.*, **4**, 7 (1961).
[2] Boone, L., *N.Y. Zool. Soc. Bull.*, **8**, 69 (1926).
[3] Boone, L., *N.Y. Zool. Soc. Bull.*, **8**, 73 (1926).
[4] Melin, G., *K. Sv. Vetensk. Akad. Handl.*, Series 3, **18**, 1 (1939).
[5] Gordan, J., *Bull. Amer. Mus. Nat. Hist.*, **108**, 255 (1956).
[6] Henderson, J. R., *Challenger Rep.*, **69**, 1 (1888).
[7] Milne Edwards, A., and Bouvier, E.-L., *Mem. Mus. Comp. Zool. Harvard*, **14**, 1 (1893).
[8] Boas, J. E. V., *Kgl. Danske Vidensk. Selsk. Biol. Medd.*, **4**, 4, 1 (1924).
[9] Borradaile, L. A., *Brit. Antarct. Terra Nova Exp., Zool.*, **3**, 3, 111 (1916).
[10] Harms, J. W., *Z. Wiss. Zool. Leipzig*, **140**, 167 (1932).
[11] Harms, J. W., *Jena Z. Naturwiss.*, **71**, 1 (1938).

Adaptive Euryhalinity in the Cyprinodont *Lebistes reticulatus* Peters

Lebistes reticulatus has always been considered as a strictly freshwater fish[1] (that is, it can tolerate only a narrow range of salt concentration in the water). In an evacuation canal, which opens in the sea, at Hann (north of Dakar), we were astonished to find numerous individuals of this species, even in spots where the concentration of sea-water was rather high. Experiments in the laboratory led us to the following conclusions:

(1) The upper limit of salinity tolerated by this species, at 20–25° C., when transferred directly from fresh water, is about 50 per cent sea-water. At such a concentration, mortality is very low (7 per cent). At a concentration of 85 per cent sea-water or higher, all fish perished within 2–3 days.

(2) Fish kept in 50 per cent or 75 per cent sea-water, for 1 wk., were transferred to 100 per cent sea-water, without any mortality resulting. During the following two months these fish were regularly observed; they seemed well and healthy, and their behaviour was apparently normal.

(3) Several series of fish were transferred successively to baths containing higher and higher concentrations of sea-water (25, 50, 75 and finally 100 per cent sea-water). They were kept for 1 wk. in each bath; the resulting mortality was nil. This seems to prove that we are dealing with a phenomenon of adaptation rather than selection.

(4) Fish adapted to sea-water were transferred directly to fresh water; no mortality resulted. This means that individuals adapted to sea-water have no need of a new adaptation to fresh water.

(5) The adaptation to sea-water is temporary, since individuals adapted to sea-water all died when transferred to fresh water and returned to sea-water within a week.

(6) A special design permitted us to adapt individuals to more and more concentrated media, by gradually increasing the sea-water content in the aquarium in which the fish were put, in such a manner that the fresh water was replaced by sea-water, within 28 or 36 hr. When fresh-water replacement was accomplished within 28 hr., all fish without exception died during the 24 hr. following. When the replacement was accomplished within 36 hr., only three individuals (out of fifty fish) died. This means that the minimum time for adaptation to sea-water is about 36 hr.

(7) Several series of 25 individuals each were adapted to sea-water during at least 3 wk.; they were transferred to fresh water and then returned again to sea-water, 24, 36, 48 or 72 hr. after. The results obtained were as follows:

Time (hr., in fresh water)	No. dead
24	none
36	4 individuals
46	8 individuals
72	20 individuals

This means that individuals begin to lose their adaptation to sea-water when kept in fresh water for about 36 hr., that is, the minimum time for adaptation to sea-water is approximately equivalent to that during which the fish keep their adaptation to sea-water.

(8) Having noticed during the previous experiments that males usually die before the females, 100 adult individuals of both sexes were transferred directly to pure sea-water. Five and a half hours after, fish began to die (especially males). Six and a half hours after they began to die, all males were already dead, but only 55 females were quite dead. The remaining females died within the following 12 hr.

We are aware of the probable existence of the factor, namely, weight of the individuals in the mortality, since the youngest adult female is usually heavier than the biggest male. However, we think that this factor is not exclusive. For the same sex (male), the histogram has shown that mortality was not a function of the weight, but represented by a Gaussian curve.

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[1] Pickford, G., and Atz, W., *N.Y. Zool. Soc. Pub.*, 156 (1955).

Effect of Temperature on *Apis indica* Workers

Recent work on the effect of environmental temperature on the European honeybee, *Apis mellifera*[1–3], has been partially repeated with two colonies of *Apis indica* brought from Ceylon by Mr. L. A. S. Perera.

Groups of 100 *A. indica* were kept in cages for three days with sugar syrup (2 parts sugar : 1 part water) and water at temperatures from 20° to 40° C., three groups being kept at each temperature; the amount of food and water consumed, the temperatures at the centres of the groups, and the number of bees which died, were recorded. The results are given in Table 1. Comparable results for *A. mellifera* are in brackets.

Table 1

Environmental temperature (° C.)	Mean temperature of groups (° C.)	Mean consumption (mm.³) per bee per day: Sugar syrup	Water	Mean No. dead at end of day 1
20	24·0 (24·9)	17·1 (31·7)	0·1 (0)	8·9 (4·0)
25	29·3 (29·6)	17·2 (21·3)	0·1 (0·3)	5·5 (1·0)
30	31·4 (30·8)	14·3 (11·5)	0·1 (0·5)	4·0 (4·0)
35	35·7 (35·0)	11·6 (18·6)	1·2 (10·1)	1·0 (3·7)
40	39·6 (39·2)	1·9 (5·5)	21·8 (16·7)	15·0 (13·8)

Groups of *A. indica* at 20° and 25° C. took similar amounts of food and were both about 4 deg. C. above environmental temperature but, in general, the lower the environmental temperature the greater the difference between it and the group temperature, and the greater the food consumption. Thus *A. indica* like *A. mellifera* responds to low temperature by increased food consumption, indicating increased metabolism, and increased production of heat. At 40° C. both species took little food but large quantities of water, reflecting a high rate of losing water. The mortality of both species was similar at the higher temperatures, but was greater for *A. indica* at the lower temperatures.

To find the temperature at which the two species enter chill coma single *A. indica* and *A. mellifera* workers were taken from their hive entrances and placed at low temperatures. Table 2 shows the numbers that moved and were still after exposure for 1 hr. All those that were still, moved again when the temperature was raised.

Table 2

Environmental temperature (° C.)	*A. indica* Moved	*A. indica* Still	*A. mellifera* Moved	*A. mellifera* Still
8	0	12	0	12
9	0	17	3	15
10	1	30	20	10
11	22	22	33	10
12	15	12	21	3
13	21	4	26	0
14	6	0	6	0

Unfortunately, the *A. indica* colonies died before much information could be obtained on the effect of previous acclimatization on chill coma temperatures. However, after acclimatization at 35° C. for 24 hr. only 6 out of 21 *A. indica* moved at 11° or 12° C., whereas 12 out of 18 *A. mellifera* moved. Thus the species differed in behaviour ($P < 0{\cdot}05$) even when acclimatized to the same temperature. Both appeared to have a higher chill coma temperature after being kept at temperatures higher than they would have experienced at their hive entrances.

Mellanby[4] found that *Cimex lectularius* (from temperate regions) was more resistant to starvation and desiccation, and could breed more successfully at low temperatures than *C. rotundatus* (from tropical regions) but found no circumstance in which *C. rotundatus* was markedly superior. Our results indicate that *A. mellifera* is more adapted to temperate climates than *A. indica*, but do not show that *A. indica* has any corresponding adaptation to the tropics.

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[1] Free, J. B., and Spencer-Booth, Yvette, *J. Exp. Biol.*, **35**, 930 (1958).
[2] Free, J. B., and Spencer-Booth, Yvette, *Bee World*, **40**, 173 (1959).
[3] Free, J. B., and Spencer-Booth, Yvette, *Ent. Exp. and App.*, **3**, 222 (1960).
[4] Mellanby, K., *Parasitology*, **37**, 111 (1935).

Effect of Ringing Cotton Stems on Content of Reducing Sugars and Insoluble Nitrogen and on Degree of Infection with *Xanthomonas malvacearum* (E.F.S.) Dowson

Hughes and Fowler[1] reported that the glucose-level of the leaves of synthesized varieties containing black-arm resistance genes B_1 or $B_2 + B_3$ was higher than that of the susceptible parent type during the first three months after sowing. Bird and Johan[2] found that girdling the main stem of a susceptible variety caused cotton plants to become more resistant to the same disease. In the present investigation the effect of ringing the main stem of cotton plants on the level of reducing sugars and insoluble nitrogen in the leaves, and its relation to infection with the angular leaf spot disease, were examined.

Plants of susceptible Domains Sakel cotton (*Gossypium barbadense* L.) were grown singly in 18-l. tins, topped when about 4 months old to induce thicker foliage, and inoculated about 4 wk. later. Two series of experiments were carried out. In the first, namely, 1957 series, inoculation was by rubbing the under-surface of the leaves with the crude suspension of *Xanthomonas malvacearum* prepared from naturally infected leaves of cotton. Twenty to thirty leaves, borne on four plants, were inoculated for each treatment (Table 1). In the second series (1958 series), inoculation was by spraying a thick water suspension of a recent isolate of *X. malvacearum* on to the leaves of the same variety of cotton. Eight plants were so inoculated in each treatment and 80–100 leaves were used for assessing the degree of infection about 4 wk. later in accordance with the grading system adopted in ref. 3. The grades were based primarily on the size and shape of the spots, with 1 representing full immunity and 12 full susceptibility.

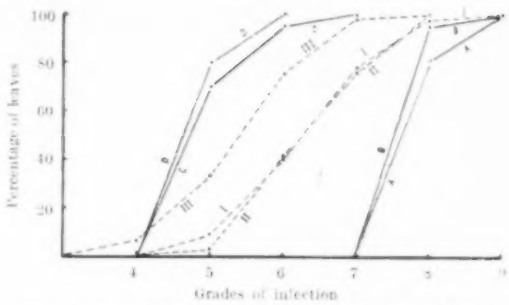

Fig. 2. Cumulative percentage of leaves showing different grades of infection (for explanation of letters and figures, see Table 1). ●——●, 1957 series; ●- - -●, 1958 series

(*a*) (*b*)

Fig. 1. Angular leaf spots on Domains Sakel cotton (1957 series); (*a*) plants not ringed, and (*b*) plants inoculated 10 days after ringing the stem

Representative samples were taken from each plant of the 1958 series for determination of reducing sugars and insoluble nitrogen contents. These samples were chosen of approximately the same size and age, and were cut just before spraying the bacterial suspension at 10–12 a.m. Maskell and Narain's modification (unpublished) of the method in ref. 4 was

Table 1. Ringing and Inoculation Treatments of 1957 and 1958 Series together with Reducing Sugars and Insoluble Nitrogen Contents of the Second Series

1957 series			1958 series				
Treatment	Ringed on	Inoculated on	Treatment	Ringed on	Inoculated on	Insoluble nitrogen gm./100 gm. dry wt.*	Reducing sugars mgm. gluc./100 gm. fr. wt.†
A	—	Oct. 12	I	—	Nov. 10	3·24	86·0
B	Oct. 12	Oct. 12	II	Nov. 10	Nov. 10	3·55	109·7
C	Oct. 12	Oct. 22	III	Oct. 30	Nov. 10	3·02	208·7
D	Oct. 12	Oct. 27					

* Means of 8 samples; $F = 1{\cdot}56$, not significant at 5 per cent level.

† Means of 8 samples; $F = 3{\cdot}64$, significant at 5 per cent level, for difference to achieve significance between treatments at $P_{0.05} = 28{\cdot}0$.

adopted for determining reducing sugars. Insoluble nitrogen was determined using a modification by Hassan[5] of the method in ref. 6.

The results of the 1957 series of inoculation experiments showed a marked increase in resistance to angular leaf spot disease 10–15 days after ringing the stems of cotton plants (Fig. 1). Plants ringed and inoculated on the same day showed no appreciable difference in the degree of infection as compared with the control (not ringed). The results of the 1958 series showed a similar trend, but were less marked (Fig. 2), probably due to differences in the method of inoculation adopted in each series. The increase in resistance coincided with a significant rise in the level of reducing sugars in the ringed plants (Table 1). Insoluble nitrogen contents, on the other hand, did not differ significantly in the three treatments. However, there was a tendency toward a lower level of insoluble nitrogen in ringed plants, which was manifested further by a pale green colour of the leaves.

As shown[7], carbohydrates increase in the leaves of stem-ringed plants while the nitrogen-level remains more or less the same. The above results show that this trend causes the plants to become more resistant to angular leaf spot disease. They show, furthermore, that a high level of reducing sugars should prevail at the time of infection. Thus, unless ringed plants are allowed a sufficient time to accumulate sugars in the leaves before inoculation, ringing would exert little or no influence on the degree of infection. The insoluble nitrogen, on the other hand, does not seem to have an effect on the degree of infection. This is in accordance with Hassan's results (unpublished).

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[1] Hughes, L. G., and Fowler, H. D., *Nature*, **172**, 316 (1953).
[2] Bird, L. S., and Joham, H. E., *Plant Dis. Rept.*, **43**, 86 (1959).
[3] Knight, R. L., and Clouston, T. W., *J. Genet.*, **38**, 133 (1939).
[4] Schaffer, P. A., and Hartman, A. F., *J. Biol. Chem.*, **43**, 349 (1920–21).
[5] Hassan, H. M., Ph.D. thesis, University of Cambridge (1953).
[6] Street, H. E., Kenyon, A. E., and Watson, G. M., *Ann. App. Biol.*, **33**, 369 (1946).
[7] Eaton, F. M., and Ergle, D. R., *Plant Physiol.*, **28**, 503 (1953).

ENTOMOLOGY

Use of an Artificial Spermatophore in the Study of Activation of Spermatozoa and Development of Spermatophores in the Cockchafer

I HAVE already described[1] the development of the reproductive organs in the male of the cockchafer (*Melolontha melolontha* L.) and the origin, development, and function of the spermatophore. The spermatophore is formed in the copulatory sac of the male while it is inserted in the bursa copulatrix of the female. The contents of the genital duct (bundles of inactivated spermatozoa, cyst cells) and the secretion of the accessory glands (the hyaline component staining green with Masson's trichrome, a granular component staining red, and basophil droplets staining blue-violet) are expelled into the copulatory sac. Within three hours of copulation, the spermatophore is encased in a protein membrane and deposited in the bursa copulatrix.

The components forming the spermatophore are at first randomly mixed. During copulation and following the deposition of the spermatophore in the bursa copulatrix, characteristic changes take place. The components of the secretion of the accessory glands are differentiated into islands of hyaline and granular substances. The spermatozoa are activated, separate from the bundles, and form clusters. They digest the hyaline substance. By this digestion numerous basophil drops begin to form. The activated spermatozoa, by means of chemotaxis, then enter the receptaculum seminis. The entire course of development has been studied by serial sections.

The suggestion of using an artificial spermatophore originated in the attempt to discover if the mechanism initiating the reactions in the spermatophore was the simple mixing of the spermatophore components or the influence of the ejaculatory duct during copulation or of the bursa copulatrix. The artificial spermatophore is prepared as follows. The contents of the dissected ejaculatory duct and the accessory glands of the male are mixed on a slide approximately in the ratio of 1 : 2 (this ratio corresponds to the ratio in natural conditions). The drop is mixed lightly and covered with a cover-slip. The mixture must be spread without any air bubbles under the entire cover-slip, the edges of which are then sealed with 'Vaseline'. It is necessary to carry out the work quickly. The entire development can then be examined by phase-contrast microscopy.

The components of the artificial spermatophore are distributed randomly when it is first made (Fig. 1). After 30 min. the differentiation of the components of the accessory glands begins. 1–2 hr. later the individual spermatozoa are activated and they move about in the hyaline substance (Fig. 2). After 2–3 hr. the spermatozoa are completely activated and concentrated in large clusters. From 6 to 24 hr. the hyaline substance gradually decreases. After 24 hr. (18° C.) when the hyaline substance is used up, movement of the spermatozoa ceases.

Artificial spermatophores not only clearly show that all the changes are entirely independent of external factors, but also make it possible to observe the entire course of development of the spermatophore *in vitro*.

When the artificial spermatophore was subjected to flowing oxygen, air and nitrogen, development of the spermatophore was found to be quickest and activation most complete in nitrogen ; air was not so

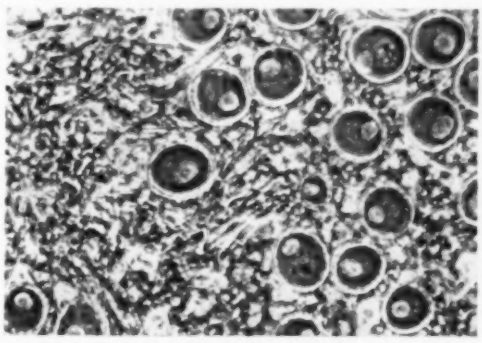

Fig. 1. Artificial spermatophore immediately following its preparation. The components of the secretion of the accessory glans and genital duct are randomly distributed. Phase contrast. (× 210)

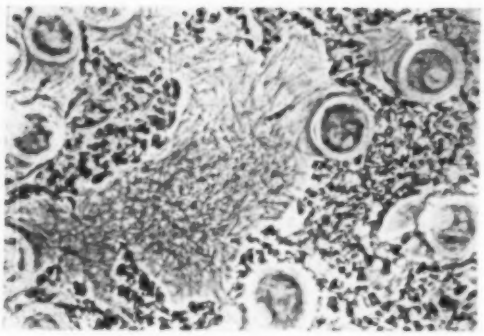

Fig. 2. Artificial spermatophore after 1–2 hr. The components of the secretion of the accessory glands are being differentiated. Individual, activated spermatozoa appear in the hyaline substance. Phase contrast. (× 210)

effective. Although a quick activation of spermatozoa takes place in oxygen, there is, however, no differentiation of the secretions of the accessory glands in oxygen, so that the spermatozoa die in about 1 hr. The mechanism of the development of the spermatophore is, therefore, adapted to the conditions in the bursa copulatrix where there is a lack of oxygen.

Experiments have shown that although oxygen itself may initiate the activation of spermatozoa, it does not do so, however, under natural conditions. Both in the artificial and natural spermatophore, the activation of spermatozoa is initiated by the hyaline substance (in making artificial spermatophores a slight activation often takes place due to contact with air). 10–15 min. after sealing the cover-slip, movement ceases. Complete activation with subsequent clustering may be observed only after differentiation of the secretion of the accessory glands.

The differentiation of the secretion is caused both by the cyst cells and by the bundles of inactivated spermatozoa, evidently due to the change in the surface tension in the spermatophore mass.

The method of making artificial spermatophores, on account of its simplicity, may be used not only in the work on special problems of the development of the spermatophore in insects, but also in some general biological problems, mainly those of activation, inactivation and nutrition of spermatozoa.

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[1] Landa, V., *Acta Soc. Ent. Czechoslov.*, **56**, 313 (1959); **57**, 297 (1960).

Termination of Pupal Diapause in the Cinnabar Moth and the Reproductive Capacity of the Resulting Females

Many thousands of pupæ of the cinnabar moth, *Tyria jacobaeae* L., from southern England, and a smaller consignment from central Italy, were introduced into Australia for the control of the noxious weed, ragwort (*Senecio jacobaea* L.), in southern Victoria. In England this moth has a strictly univoltine life-cycle[1] that includes an obligatory pupal diapause[2] lasting for an average of 270 days. Because of this diapause[3], difficulties were expected in synchronizing emergence of the moths with the Australian summer—for this would require diapause to be terminated in less than 150 days or extended to at least 450 days.

The pupæ were stored at 1–3° C. between layers of moist sphagnum. It was hoped that diapause could be terminated by chilling pupæ and later exposing them to higher temperatures. All pupæ were so treated except one small batch of the Italian consignment which was stored at room temperature (range 5–15° C.).

At the beginning of the Australian summer, most of the pupæ were transferred to an insectary where temperatures ranged from 15° to 35° C., but only 6·1 per cent of the English and none of the Italian pupæ produced moths. Strangely enough, 50 per cent of the Italian pupæ kept at room temperature emerged. However, very few of the progeny of these Italian moths completed the larval stage, whereas those from adults of English origin were reasonably successful. Dissections made at the end of summer showed that most of the English pupæ were still alive. The remainder were returned to a cold room and stored until the following year when, after 500 days in diapause, they were again subjected to temperatures in the range of 15–35° C. This second exposure produced an 8·6 per cent emergence.

Three groups of pupæ were set aside to study the effect of temperature and duration of exposure on emergence of adults (see Table 1). Group *B* was held continuously in the cold room at 1–3° C. for 270 days. Group *A* was similarly chilled for 50 days, and then exposed to temperatures within the range 20–48° C. for 150 days. Group *C* was chilled for 90 days, and then held at 15–35° C. for 150 days. Both *A* and *C* were then returned to the cold room. When the pupæ had been in diapause for 300 days, 2–6 batches, each of 25 pupæ, were exposed to 20° C. Samples were drawn from each experimental group at intervals of three weeks. The emergences that resulted are summarized in Table 1. The results for Group *A* suggest that abnormally high temperatures alternating

Table 1. Emergence of Moths after Exposure to Different Temperature Régimes

Groups	No. of replicates	Total No. of pupæ	Details of treatment*		Duration of pupal stage (days) 302	323	344	365	386	407	428	449	470	491	512	533	554	575	Total percentage emerged
A	14	350	50 days at 1–3° C. 150 " " 20–48° C. 135 + " " 1–3° C. remainder at 20° C.					44	60	38	56	40	34	62					48
B	52	1,300	270 + days at 1–3° C. without interruption remainder at 20° C.	Mean percentage emerged	81	72	51	50	37	36	38	21	8	3	5	4	2		31
C	84	2,100	90 days at 1–3° C. 150 " " 15–35° C. 30 + " " 1–3° C. remainder at 20° C.		53	47	49	55	57	62	62	54	46	50	41	40	25	21	58

* The pupæ were in transit for 32 days before the treatments named were commenced.

Table 2. Reproductive Capacity of the Cinnabar Moth

Stock	No. of females tested	No. of diapause (days)	Time of emergence	Percentage of females ovipositing	No. of eggs laid	No. of eggs hatched per female
English	40	150	Jan. 1955	6·2	75	10
Italian	20	150	Jan. 1955	8·5	94·4	29·9
English	100	270	May 1955	8·6	95·7	60·1
English	100	360	Aug. 1956	7·9	81·5	37·6
English	100	420	Oct. 1956	7·8	60·2	15·8
English	100	500	Jan. 1957	8·0	58·9	8·1
Australian	50	270	Dec. 1957	7·8	155·1	74·7

with cold treatment produce an erratic although tolerably high emergence of adults. Prolonged cold treatment (group *B*) was apparently detrimental to the pupæ, as the gradually decreasing values suggest. This was also reflected in the statistical analysis, where emergence from group *B* was significantly different from that of group *A* or *C*. In group *C*, receiving alternately cold and warm conditions, relatively high emergence (40 per cent) was recorded after 533 days, that is, after the insects had spent almost twice the normal period in diapause. The sharp contrast in the results from the English and Italian consignments suggests that they may have comprised two different strains of insects. The English strain proved itself to be the more suitable for the climate of Gippsland, Victoria.

Three factors influencing the reproductive capacities of the moths that emerged under various treatments are summarized in Table 2. All three factors—percentage females ovipositing, number of eggs laid and number of eggs hatched per female—were optimal or near optimal when pupal diapause extended for the normal period of 270 days. In the case of the English stock, however, this corresponded to emergence during the Australian winter. A diapause period of 150 days (that is, emergence in the first Australian summer) resulted in less-favourable reproductive capacity, as also did such longer diapause periods as 360, 420 or 500 days. Although females of the Italian stock laid more eggs than those of the English stock, and their viability was also appreciably higher, very few of their progeny completed larval development. The differences in fecundity associated with the duration of diapause were found to be significant.

To sum up, although termination of diapause in *T. jacobaeae* was more successful when this stage was prolonged rather than shortened, the fecundity of the moths produced was adversely affected by long periods of diapause.

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[1] Cameron, Ewen. *J. Ecol.*, **23**, 2, 265 (1935).
[2] Lees, A. D., Camb. Mon. Exp. Biol., No. 4 (1955).
[3] Andrewartha, H. G., *Biol. Rev.*, **27**, 50 (1952).

BACTERIOLOGY

Interspecific Induction of Transformation of Bacteria with Respect to Phage-susceptibility

Several examples of bacterial transformation have been reported since the discovery of the phenomenon by Griffith[1]. Among the properties found to be transformed, besides synthesis of the capsular polysaccharide antigens, are drug-resistance and enzymic capacities[2]. In work concerned with the host-specificity of a phage (*S-a*) attacking an amylase-forming bacterium, *Bacillus subtilis* var. *amyloliquefacus*[3], we have tried to transform a non-susceptible organism into a susceptible one. This communication describes the successful results of such an experiment.

First, a trial was made to obtain a susceptible organism through mutation of non-susceptible strains of the *subtilis* group, but with little success, because of the difficulty of discriminating between the wild form and any mutants which might have been produced. A coloured organism, *Bacillus megaterium roseus*, was used in the next trial, in view of the ease in overcoming this difficulty. In fact, several colourless mutants were obtained by the application of a cell-free extract prepared from the susceptible organism. Then tests were made to examine these mutants for their susceptibility to the phage under investigation, which led to the discovery among them of one susceptible mutant. Experimental results will be described briefly now.

The transforming agent was prepared from the cells of the susceptible organism (*Bacillus subtilis* var. *amyloliquefacus*) in the logarithmic phase of its growth (4–5 hr. after inoculation). The bacterium was incubated in a nutrient broth medium in a reciprocal shaker at 37° C. Bacterial cells were gathered by centrifugation, washed three times in 0·9 per cent physiological saline and resuspended in about 10 ml. of the same saline. The cells were disrupted with a sonic oscillator operating at 9–10 kc./s. for 15 min. at 5° C. Cell fragments were collected by centrifugation (10,000*g* 20 min.), the supernatant filtered through a Seitz filter and used as transforming agent after a test for absolute sterility. On the other hand, the cells of *Bacillus megaterium roseus* in the logarithmic phase of growth were incubated at 37° C. in a broth medium with the addition of the transforming agent (final concentration, about 20 μgm. DNA per ml., as determined by the method of Webb and Levy)[4]. At intervals, platings (broth agar) were made to detect the formation of mutants, using several dilutions of aliquots taken from the culture. After 16–18 hr. of incubation, the occurrence of transformation was actually detected, as revealed by the appearance, on later plating, of discoloured mutant colonies at a frequency of approximately one in 10^3–10^4 genuine, pink-coloured colonies. Some of these mutants were pale-yellow in colour, some colourless. No change in morphological characteristics (size and shape) of the cell was discovered in either of them. Each colony of the mutants, as discerned by the naked eye, was separately tested for its susceptibility to phage *S-a* by plating the cells with the addition of appropriate amounts of the phage. With most of the mutants, the result was negative, but there was a colourless strain which showed evident plaque-formation in the test. Multiplication of the phage afterwards was also confirmed by several successive transplantations of the plaques on the colourless mutant.

No back-mutation has been detected, offspring obtained by subculturing the mutant strain, when tested, always exhibiting the acquired characteristics of the mutant, white colour of the colony and susceptibility to phage.

The formation of mutant, either coloured or colourless, was found to be reproducible, its frequency being augmented to some extent by increasing the concentration of the transforming agent. On adding still

larger amounts of the inducing agent, however, a state of saturation was obtained, corresponding to a frequency of one mutant colony per 10^3 normal, pink-coloured colonies.

These results are best accounted for by assuming a transformation of the originally phage-resistant, pink-coloured strain of *Bacillus megaterium roseus*, into a phage-susceptible, colourless mutant.

The role of the bacterial extract in inducing the transformation in question is indicated evidently by the fact that no single example of formation of susceptible mutant has ever been observed without the addition of the extract. The colourless mutants appearing, although far less frequently, as a result of spontaneous mutation (that is, without any addition of transforming agent) were also tested for phage-susceptibility but always with negative results. This transforming agent was also found not to be replaceable with extracts prepared in a similar way but from other phage-resistant strains of bacteria (for example, *Bacillus mesentericus vulgatus* Piorkowisky and *Bacillus subtilis NRRL* 558). As to the actual nature of the transforming principle contained in the effective extract, any decisive account will be premature. In view of the finding, however, that the inducing activity of the extract is abolished by treating it with deoxyribonuclease, there is a possibility that a specific deoxyribonucleate is involved (prolonged treatment with other hydrolysing enzymes, such as ribonuclease and trypsin, had no effect on the activity).

In conclusion, it may be stated that the facts reported above will be of some importance in disclosing the possibility of interspecific induction of transformation in bacteria mediated by a soluble transforming principle.

The present work was initiated by the advice given by Prof. A. Takamiya, University of Tokyo, to whom our thanks are due.

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[1] Griffith, F., *J. Hyg.*, **27**, 113 (1928).
[2] Ephrussi-Taylor, H., *Adv. Virus Res.*, **3**, 275 (1955).
[3] Fukuda, S., *J. Gen. Appl. Microbiol.*, **7**, 1 (1961).
[4] Webb, J. M., and Levy, H. B., *J. Biol. Chem.*, **213**, 107 (1955).

Chitinoclastic Activity in the Luminous Bacteria

There would appear to have been no reports in the literature on luminous bacteria of chitinoclastic activity in this group[1] nor, during attempts to obtain chitinoclastic bacteria from marine environments, have luminous bacteria been isolated[2,3]. Indeed, in a recent publication[4] it is stated that members of the genus *Photobacterium* "do not or are not known to hydrolyse . . . chitin". It is, consequently, of importance to report observations made some time ago on the chitinoclastic activity of a variety of luminous bacteria, all the species available at present having been examined.

Chitin was prepared from crab shells by the method of Benton[5], and following precipitation from sulphuric acid by potassium hydroxide and washing it was added to a basal medium consisting of glucose 0·1 per cent, peptone 0·1 per cent, dipotassium hydrogen phosphate 0·005 per cent and agar 1·5 per cent in sea-water, to give a milky opacity. The cultures were streaked on the surface of this medium, incubated at 20° C. for up to 14 days, and examined for the production of a zone of clearing of the chitin around the bacterial growth.

Table 1. Chitinoclastic Activity of Various Species of Luminous Bacteria

Species	No. of strains examined	Source	No. of strains exhibiting chitinoclastic activity
Photobacterium splendidum	1	Delft collection	1
Ph. sepiae	1	Delft collection	1
Vibrio albensis	1	Delft collection	1
Ph. harveyi	1	Delft collection	1
Ph. harveyi	1	Prof. Johnson, Princeton	1
Ph. pierantonii	1	Delft collection	1
Ph. fischeri	1	Prof. Johnson, Princeton	1
Ph. phosphoreum	1	Delft collection	1
Ph. phosphoreum	1	Prof. Johnson, Princeton	1
Ph. phosphoreum	10	Fish intestinal contents, North Sea	8
Ph. phosphoreum	3	Fish intestinal contents, Dr. Georgala, Cape Town	3
Ph. phosphoreum	12	Marine animals, Drs. Iijima, Yosaki, Japan	11
Unidentified, similar to *Ph. fischeri*	29	Fish intestinal contents, North Sea	21
Unidentified possibly new species	1	Fish intestinal contents, North Sea	1

Table 1 shows the strains examined, their source, and their ability to digest chitin under the experimental conditions used. The cultures recorded as negative were not re-examined nor was incubation continued beyond 14 days. It would appear that chitinoclastic activity is widespread among the luminous bacteria, even the freshwater species, *Vibrio albensis*, exhibiting it, and it is, consequently, perhaps not unreasonable to suggest that chitinoclastic activity, to a greater or lesser degree, may be a constant characteristic of this group of bacteria.

The part that the luminous bacteria may play in the degradation of chitin in Nature is obscure. Certain members have been found to be almost invariably present in and frequently forming a large part of the bacterial flora of the intestines of a variety of fish caught in the Arctic, North Sea and around the British Isles. Crustacea may form a not inconsiderable portion of the diet of such fish, and it has been suggested that symbiotic bacteria may aid animals in the digestion of chitin[3]. It is probable, however, that much of the chitin in the oceans finds its way to the bottom deposits and there is little, if any, information concerning the occurrence of luminous bacteria in this environment.

The work described in this communication was prepared as part of the programme of the Department of Scientific and Industrial Research.

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[1] *Bergey's Manual of Determinative Bacteriology*, seventh ed., edit. by Breed, R. S., Murray, E. G. D., and Smith, N. S. (Baillière, Tindall and Cox, Ltd., London, 1957).
[2] Zobell, C. E., and Rittenberg, S. C., *J. Bacteriol.*, **35**, 275 (1938).
[3] Campbell, L. L., and Williams, O. B., *J. Gen. Microbiol.*, **5**, 894 (1951).
[4] Skerman, V. B. D., *A Guide to the Identification of the Genera of Bacteria* (The Williams and Wilkins Co., Baltimore, 1959).
[5] Benton, A. G., *J. Bacteriol.*, **29**, 449 (1935).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Tuesday, June 6

OPERATIONAL RESEARCH SOCIETY, and the BRITISH INSTITUTE OF MANAGEMENT (at the Connaught Rooms, Great Queen Street, London, W.C.2), at 9.30 a.m.—Conference on "Operational Research".

UNIVERSITY OF LONDON (in the Clinical Lecture Theatre, Middlesex Hospital Medical School, Mortimer Street, London, W.1), at 4.15 p.m.—Sir William Ogg: "Soils, Crop Nutrition and Health"* (Sanderson Wells Lecture).

UNIVERSITY COLLEGE (in the Physiology Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. G. P. Lewis: "Bradykinin, its Chemistry, Pharmacology and Role in Physiological and Pathological Reactions".*

UNIVERSITY OF LONDON (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 5.45 p.m.—Prof. F. E. Zeuner: "Archæological Problems of the Canary Islands".*

Wednesday, June 7

UNIVERSITY OF LONDON (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. P. Wildy: "Architecture of Viruses".*

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. G. R. Coope: "A Northern Insect Fauna from a Terrace of the River Avon at Fladbury, Worcestershire": Dr. H. J. Sullivan: "Distribution of Miospores through Coals and Shales of the Coal Measures Sequence Exposed in Werndduu Claypit, Caerphilly, South Wales".

Thursday, June 8

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. D. J. Bradley: "The Rapid Measurement of Intensity with an Oscillating Fabry-Perot Spectrometer: Isotope Abundance in Mercury": Mr. A. H. Cook: "Precise Measurements of the Density of Mercury at 20° C. II: Content Method".

ROYAL INSTITUTION OF NAVAL ARCHITECTS (at 10 Upper Belgrave Street, London, S.W.1), at 4.45 p.m.—Mr. J. Clarkson: "The Behaviour of Deck Stiffening under Concentrated Loads" and "Uniform Pressure Tests on Plates with Edges Free to Slide Inwards".

MINERALOGICAL SOCIETY (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Scientific Papers.

INSTITUTE OF PHYSICS AND THE PHYSICAL SOCIETY, ACOUSTICS GROUP (in the Physics Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7), at 5.30 p.m.—Annual General Meeting, followed by Dr. W. L. Nyborg (University of Vermont): "Biophysical Applications of Non-linear Acoustics".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

RESEARCH WORKER IN GLACIOLOGY—Dr. Hal Lister, Lecturer in Polar Studies, King's College, Newcastle-upon-Tyne 1 (June 8).

ASSISTANT LECTURER IN EXPERIMENTAL PHYSICS, to collaborate in research in high energy nuclear physics using the accelerators of C.E.R.N. and the Rutherford Laboratory—The Secretary to Council, Westfield College (University of London), Hampstead, London, N.W.3 (June 9).

ASSISTANT LECTURER and a LECTURER IN PHYSICS—The Registrar, The University, Nottingham (June 10).

LECTURER or ASSISTANT IN GEOLOGY—The Secretary of University Court, The University, Glasgow (June 10).

RESEARCH ASSISTANT IN MATHEMATICAL STATISTICS IN THE DEPARTMENT OF APPLIED MATHEMATICS—The Registrar, The University, Liverpool (June 10).

SCIENTIFIC OFFICER (graduate with first- or second-class honours in mathematics with statistics, or a diploma in statistics) IN THE STATISTICS SECTION, for duties mainly concerned with the design and analysis of field experiments—The Secretary, Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (June 10).

RESEARCH ASSISTANT (with a degree qualification in physics, and preferably an interest in high vacuum techniques and/or electronics) IN THE DEPARTMENT OF PHYSICS AND MATHEMATICS, College of Technology, Liverpool, to participate in a research programme dealing with electron impact and corrosion—The Director of Education, City of Liverpool Education Committee, 14 Sir Thomas Street, Liverpool 1 (June 12).

DEMONSTRATOR (with a good honours degree in biology or zoology and preferably with experience in practical genetics) IN THE BIOLOGY DEPARTMENT—The Registrar, University College of North Staffordshire, Keele, Staffs (June 15).

ASSISTANT LECTURER IN THE GEOLOGY DEPARTMENT, to teach mineralogy and encourage research in this field—The Registrar, King's College (University of London), Strand, London, W.C.2 (June 16).

GEOCHEMIST (with a special interest in spectrography and preferably previous experience of the geochemistry of sedimentary rocks) IN THE DEPARTMENT OF GEOLOGY—The Registrar, The University, Sheffield (June 16).

LECTURER IN BIOCHEMISTRY—The Secretary of University Court, The University, Glasgow (June 16).

ASSISTANT LECTURER (Grade III) IN BOTANY—The Registrar, The University, Bristol 8 (June 17).

PROFESSOR OF BOTANY—The Secretary and Bursar, University College, Earlsfort Terrace, Dublin, Republic of Ireland (June 17).

RESEARCH ASSISTANT (graduate in chemistry or biochemistry) IN CHEMISTRY, to work in the Department of Chemistry of the Faculty of Science under the direction of Dr. C. R. Barker on the chemistry and biochemistry of nucleic acids—The Registrar, The University, Manchester 13 (June 17).

RESEARCH ASSISTANT IN THE DEPARTMENT OF MATHEMATICS AND PHYSICS, to take part in research work on the microwave properties of certain magnetic oxides and to undertake a certain amount of teaching—The Registrar, College of Technology, Park Road, Portsmouth (June 17).

RESEARCH ASSOCIATE (APPLIED MATHEMATICIAN) IN THE DEPARTMENT OF THEORETICAL MECHANICS (Faculty of Engineering)—The Registrar, The University, Bristol 8 (June 17).

VIROLOGIST, Experimental Officer (male, with a degree in botany or agriculture and experience of plant virus techniques), to co-operate in research aimed at developing virus resistance in the potato—The Secretary, Scottish Plant Breeding Station, Pentlandfield, Roslin, Midlothian (June 17).

LECTURER (Grade II) IN THE DEPARTMENT OF MECHANICAL ENGINEERING—The Registrar and Secretary, The University, Bristol (June 19).

ASSISTANT LECTURER IN BIOCHEMISTRY IN THE DEPARTMENT OF AGRICULTURAL BIOCHEMISTRY—The Registrar, University College of Wales, Aberystwyth (June 24).

LECTURER IN PHARMACOLOGY IN THE DEPARTMENT OF PHARMACOLOGY AND THERAPEUTICS—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (June 24).

RESEARCH ASSISTANT (man or woman graduate of any university) for freshwater phytoplankton investigations—The Principal, Royal Holloway College (University of London), Englefield Green, Surrey (June 24).

LECTURER (with a knowledge of selection and breeding of Nigerian grasses) IN PLANT BREEDING IN THE DEPARTMENT OF AGRICULTURE, University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (June 25).

LECTURER or ASSISTANT LECTURER IN PHYSIOLOGY—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (June 30).

LECTURERS (2) IN CHEMISTRY at Victoria University of Wellington, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, W.C.1 (New Zealand and London, June 30).

LECTURER or ASSISTANT LECTURER IN PHYSICAL METALLURGY—The Assistant Registrar (Science), The University, Edgbaston, Birmingham 15 (July 1).

RESEARCH STUDENTS (with the degree of Bachelor or Master of a British University other than Manchester) IN SCIENCE—The Registrar, The University, Manchester 13 (July 1).

SENIOR LECTURER (experienced in clinical biochemistry as well as in administration and capable of directing the clinical pathology service of a general hospital of approximately six hundred beds) IN CLINICAL PATHOLOGY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, July 7).

SENIOR LECTURER or LECTURER IN SCIENTIFIC THOUGHT IN THE SCHOOL OF PHILOSOPHY, University of New South Wales—Agent-General for New South Wales, 56–57 Strand, London, W.C.2 (Australia and London, July 14).

ASSISTANT PROFESSOR IN BIOPHYSICS and an ASSISTANT PROFESSOR IN METEOROLOGY—G. M. Shrum, Physics Department, University of British Columbia, Vancouver 8, B.C., Canada.

DISTILLERS COMPANY RESEARCH STUDENT IN THE DEPARTMENT OF CHEMICAL ENGINEERING, for work leading to a higher degree on the kinetics of the gaseous oxidation of aromatic hydrocarbons—The Secretary, University College, Gower Street, London, W.C.1.

GRADUATE (with a good first degree in chemistry, physics or chemical engineering) IN THE CHEMICAL ENGINEERING DEPARTMENT, to undertake research for a higher degree on some aspects of flame propagation—Dr. J. H. Burgoyne, Chemical Engineering Department, Imperial College of Science and Technology, London, S.W.7.

HEAD OF THE DEPARTMENT OF PARASITOLOGY, The Secretary, Animal Diseases Research Association, Moredun Institute, Gilmerton, Edinburgh 9.

HEAD (with high academic qualifications in mathematics and teaching and research or industrial experience) OF THE DEPARTMENT OF MATHEMATICS—The Principal, Huddersfield College of Technology, Huddersfield.

LECTURER IN MATHEMATICS; and an ASSISTANT, Grade B, IN MATHEMATICS—The Registrar (Department *F*), Bradford Institute of Technology, Bradford 7.

LOW TEMPERATURE PHYSICIST (Assistant Professor, Associate Professor or Professor) IN THE LOW TEMPERATURE LABORATORY—G. M. Shrum, Physics Department, University of British Columbia, Vancouver, B.C., Canada.

POSTDOCTORAL FELLOW, for work in the field of photochemical reactions in the alkali halides—Dr. P. W. M. Jacobs, Chemistry Department, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7.

POSTDOCTORAL RESEARCH FELLOW, for research in gas kinetics—Dr. H. M. Frey, Chemistry Department, The University, Southampton.

READER (with high academic qualifications and considerable teaching and research experience in any field of botany or zoology) IN BIOLOGY—The Registrar (Department *F*), Bradford Institute of Technology, Bradford 7.

SCIENTIFIC OFFICER or SENIOR SCIENTIFIC OFFICER (honours graduate in chemistry or biochemistry) IN THE PHYSIOLOGY DEPARTMENT, to study the isolation and properties of various enzymes from the mammary gland and milk—The Secretary, The National Institute for Research in Dairying (University of Reading), Shinfield, near Reading, quoting Ref. 61/16.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The Neurophysiological Aspects of Hallucinations and Illusory Experience. By W. Grey Walter. (Fourteenth Frederic W. H. Myers Memorial Lecture, 1960.) Pp. 24. (London: Society for Psychical Research, 1960.) 2s. net. [203

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 61: The Care and Management of Breeding Bulls. Pp. 7. Leaflet No. 70: Ringworm. Pp. 2. (Belfast: Ministry of Agriculture, 1961.) [203

The United Steel Companies Limited. Review of Progress: a Report for Employees. Pp. 44. (Sheffield: The United Steel Companies Limited, 1961.) [203

Department of Scientific and Industrial Research. Instruments in the Factory. Pp. 12. (London: Department of Scientific and Industrial Research, 1961.) [203

International Aid for Economic Development—Possibilities and Limitations. By Dr. V. K. R. V. Rao. (Eighteenth Montague Burton Lecture on International Relations.) Pp. 29. (Leeds: The University, 1960.) 6*d*. [203

Annual Report of the National Oceanographic Council, 1 April, 1959–31 March, 1960. Pp. v + 42 + 7 plates. (Cambridge: At the University Press, 1960.) 5*s*. net. [203

The National Union of Teachers Annual Guide to Careers for Young People, March, 1961. Pp. viii + 80. (London: National Union of Teachers, 1961.) 3*s*. [203

The Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom. Code of Practice for the Protection of Persons Exposed to Ionizing Radiations in University Laboratories. Pp. v + 72. (London: Association of Universities of the British Commonwealth, 1961.) 3*s*. 6*d*. [203

The Macaulay Institute for Soil Research. Annual Report, 1959–1960. Pp. 52. (Craigiebuckler, Aberdeen: Macaulay Institute for Soil Research, 1961.) [203

Planning, Vol. 27, No. 456 (20 March, 1961): The Promotion of Economic Growth. Pp. 57–80. (London: Political and Economic Planning, 1961.) 3*s*.

Educational Television: a Survey and a Plan. By John Wellens. Pp. 44 + 8 plates. (Guilsborough, near Northampton: John Wellens (ITT), Ltd., The Sun House, 1961.) 5*s*. [203

The Science of Continuously Operating Systems. By Prof. K. G. Denbigh. (Inaugural Lecture, 1 November, 1960.) Pp. 18. (London: Imperial College of Science and Technology, 1960. Distributed by The Modern Book Co. Ltd., 19 Praed Street, W.2.) 5*s*. [203

Central Youth Employment Executive. Choice of Careers, No. 103: Art and Design. Pp. 56. (London: H.M. Stationery Office, 1960.) 2*s*. net. [203

Science and the Future of Britain. (A Labour Party *Looking Ahead* Pamphlet.) Pp. ii + 46. (London: The Labour Party, 1961.) 2*s*. [203

General Register Office. The Registrar General's Statistical Review of England and Wales for the year 1959. Part 2: Tables, Population. Pp. x + 181. (London: H.M. Stationery Office, 1960.) 11*s*. 6*d*. net. [203

Forestry Commission. Forest Record No. 44: A Creosoting Plant at Thetford Chase. By D. Small. Pp. 28. 2*s*. 6*d*. net. Forest Record No. 46: Group Dying of Conifers. By J. S. Murray and C. W. T. Young. Pp. 19 + 12 figures. 3*s*. net. (London: H.M. Stationery Office, 1960 and 1961.) [203

Other Countries

Berichte des Deutschen Wetterdienstes. Nr. 71 (Band 10): Die Meteorologischen Verhältnisse auf der Flugstrecke Deutschland—Südamerika. Von Herbert Reguła. Pp. 26. 5.25 D.M. Nr. 72 (Band 10): Wissenschaftliche Beobachtungen auf dem Nordostland von Spitzbergen 1944–1945. Von Wilhelm Dege. Pp. 134. (Offenbach a.M.: Selbstverlag des Deutschen Wetterdienstes, 1960.) [133

Sandia Corporation. Sandia Corporation Reprints Monographs, and Research Colloquia—Title List. Pp. 22. (Albuquerque, New Mexico: Sandia Corporation, 1960.) [133

World Meteorological Organization. Technical Note No. 34: The Airflow Over Mountains: Report of a Working Group of the Commission for Aerology. Edited and Co-ordinated by M. A. Alaka. Pp. v + 135. (W.M.O.—No. 98, TP 43.) (Geneva: World Meteorological Organization, 1960.) 22 Swiss francs. [133

Museum of Comparative Zoology at Harvard College. Breviora, No. 127 (December 19, 1960): Notes on the Cranial Anatomy of *Xeredemur*. By E. L. Simons and D. E. Russell. Pp. 14. No. 128 (December 20, 1960): Size of Endoceroid Cephalopods. By Curt Teichert and Bernhard Kummel. Pp. 7. No. 129 (December 21, 1960): Type and Type Locality of the Gulf Coast Spiny Softshell Turtle *Trionyx spiniferus asper* (Agassiz). By Robert C. Webb. Pp. 8 + 2 plates. No. 130 (December 22, 1960): The Mechanisms of Carapacial and Plastral Hinges in Chelonians. By R. V. Shah. Pp. 13. No. 131 (December 30, 1960): A Second Record of the Fossil Rodent *Palaeotricos* Wood. By Craig C. Black. Pp. 3. No. 132 (December 30, 1960): The Status of *Sciuravidavus notus*, with Comments on the Distribution of *S. Spatator* and *S. Sabanus*. By Wayne King. Pp. 5. Bulletin of the Museum of Comparative Zoology at Harvard College, Vol. 123, No. 6: On Burmese Earthworms of the Family Megascolecidae. By G. E. Gates. Pp. 201–282. Vol. 123, No. 7: Middle Triassic Nautiloids from Sinai, Egypt, and Israel. By Bernhard Kummel. Pp. 283–302 + 4 plates. Annual Report of the Director of the Museum of Comparative Zoology at Harvard College, 1958–1959. Pp. 26. (Cambridge, Mass.: Museum of Comparative Zoology at Harvard College, 1960.) [133

Instituto Antartico Argentino, Buenos Aires. Contribuciones, No. 31: La Campana Antartico 1957–58. Por Alberto P. Larbacette. Pp. 22. No. 38: Notas Biologicas sobre el Pinguin de Adelia. Por Ricardo Novatti. Pp. 32. No. 45: Estudios Microbiologicos sobre Animales Antarticos. Por Dr. John McNeill Sieburth. Pp. 19. Publication No. 7: Meteorologia Descriptiva del Sector Antartico Sudamericano. Por Werner Schwerdtfeger, Luis Maria de la Canal, y Jorge Schelten. Pp. 425. (Buenos Aires: Instituto Antartico Argentino, 1959.) [133

State of California: Department of Fish and Game. Fish Bulletin No. 110: A Study of the Yellowtail *Seriola dorsalis* (Gill). By John L. Baxter and a Staff of Associates. Pp. 96. Fish Bulletin No. 111: The Marine Fish Catch of California for the year 1959. By the Biostatistical Section, Marine Resources Operations. Pp. 44. Fish Bulletin No. 112: Relationships of some Marine Organisms of the Northeast Pacific to Water Temperatures, particularly during 1957 through 1959. By John Radovich. Pp. 62. (Sacramento: Printing Division, Documents Section, State of California, 1960 and 1961.) [133

United Arab Republic: Ministry of Industry, Geological Survey and Mineral Research Department. Paper No. 5: Contribution to the Geology and Mineralogy of the Hammash Copper Deposits, South Eastern Desert of Egypt. By G. A. Moustafa and M. E. Hilmy. Pp. iv + 14. P.T. 10. Paper No. 6: Cassiterite-Wolframite Mineralisation near Gebel El-Mueilha, Eastern Desert of Egypt. By M. F. El-Ramly, M. Kamal Akaad, and D. M. Al-Far. Pp. iv + 19. P.T. 20. Paper No. 7: Potassium-Argon Ages of Some Rocks from the Eastern Desert of Egypt. By Riad A. Higazy and M. F. El-Ramly. Pp. ii + 18. P.T. 15. Paper No. 8: The Basement Complex in the Central-Eastern Desert of Egypt between Latitudes 24° 30′ and 25° 40′ N. By M. F. El-Ramly and M. Kamal Akaad. Pp. iii + 35. P.T. 50. (Cairo: Ministry of Industry, Geological Survey and Mineral Research Department, 1958, 1959 and 1960.) [133

Tokyo Astronomical Observatory. Tokyo Astronomical Bulletin (Second Series), No. 128 (June 20, 1960): Precise Determination of Travel Time of Radio Signals between Hawaii and Tokyo. By Shigetaka Iijima, Goro Shibutani and Sadami Katahara. Pp. 1555–1604. No. 129 (March 25, 1960): Meridian Observation of Right Ascension of Moon's Limb made with Repsold Transit Instrument. Report No. 4. By K. Tuzi and K. Nagane. Pp. 1606–1619. No. 131 (July 20, 1960): Meridian Observations of the Right Ascensions of the Moon and Planets during the year 1959. By S. Nakano, H. Yasuda and H. Hara. Pp. 1645–1652. No. 132 (June 29, 1960): Travel Time of Radio Signals between Buenos Aires and Tokyo which are located very near the Antipodal Points with each other. By S. Iijima and K. Fujiwara. Pp. 1653–1678. No. 133 (October 15, 1960): Approximate Positions of Artificial Satellites obtained with the Baker-Nunn Schmidt Camera (4). Observation period—1959, Oct.–Dec. By the Sky Patrol Section of the Tokyo Astronomical Observatory. Pp. 1679–1694. (Tokyo: Tokyo Astronomical Observatory, 1960.) [133

Republic of Egypt: Ministry of Commerce and Industry, Mineral Resources Department, Geological Survey of Egypt. Geology of El-Shalul: El-Bakriya District (Barramiya West Sheet). By A. H. Sabet and M. A. Z'aatout. Pp. xi + 75 + 15 plates. (Cairo: Ministry of Commerce and Industry, Mineral Resources Department, 1955.) P.T. 140. [133

Forschungsberichte des Landes Nordrhein-Westfalen. Nr. 933: Die Vernebelung Schmelzbarer Festkörper mit Ultraschall. By Klaus Stamm. Pp. 24. 9.20 D.M. Nr. 944: Nitrierungdünner Stahlschichten mit Hilfe einer Glimmentladung. By Günter Waidmann. Pp. 50. 16.30 D.M. (Köln und Opladen: Westdeutscher Verlag, 1960.) [143

East Africa High Commission. East African Institute for Medical Research—Report 1959–1960. Pp. ii + 36. (Mwanza: East African Institute for Medical Research, 1960.) [143

Metropolitan Life Insurance Company, New York. Statistical Bulletin, Vol. 42 (January 1961): Fifty Years of Health Progress. Large Population Gains in the United States and Canada. Pp. 12. (New York: Metropolitan Life Insurance Company, 1961.) [143

Annals of the Natal Museum, Vol. 15, Part 9: Neue Spezies von *Notiochagus* Gory (Discolomidae, col.). Von Hans John. Pp. 93–98. 6*s*. net. Vol. 15, Part 10: *Gamasellinhis*, a New Subgenus of the Genus *Cyrtolaelaps* Berlese (Acarina: Mesostigmata: Rhodacaridae). By P. A. J. Ryke. Pp. 99–108. 6*s*. net. Vol. 15, Part 11: Records and Descriptions of Blepharoceridae, Erinnidae and Rhagionidae from South Africa (Diptera). By B. R. Stuckenberg. Pp. 109–124. 6*s*. net. (Pietermaritzburg: Natal Museum, 1961.) [203

United States Department of Agriculture. Agricultural Research Service, Agriculture Handbook No. 182: The Mosquitoes of Alaska. By C. M. Gjullin, R. I. Sailer, Alan Stone, and R. V. Travis. Pp. ii + 98. (Washington, D.C.: Government Printing Office, 1961.) 45 cents. [203

Reports on the Scientific Results of the "Michael Sars" North Atlantic Deep-Sea Expedition, 1910. Vol. 4, Part 2, No. 8: Isopsendyli. 2: Heteroprotodermi from the "Michael Sars" North Atlantic Deep Sea Expedition, 1910 (with Addenda and Corrigenda to Isospondyli 1 and 2). By Einar Koefoed. Pp. 15 + 1 plate. (Bergen: The University, 1960.) [203

Government of Pakistan: Ministry of Industries. Report of the Scientific Commission of Pakistan. Pp. iv + 102. (Karachi: Government of Pakistan, Ministry of Industries, 1960.) [203

Institut Royal Météorologique de Belgique. Observations Ionosphériques—Station de Dourbes, Juillet 1959. Pp. 26. Août 1959. Pp. 26. Septembre 1959. Pp. 26. Octobre 1959. Pp. 26. Novembre 1959. Pp. 26. (Bruxelles: Institut Royal Météorologique de Belgique, 1961.) [203

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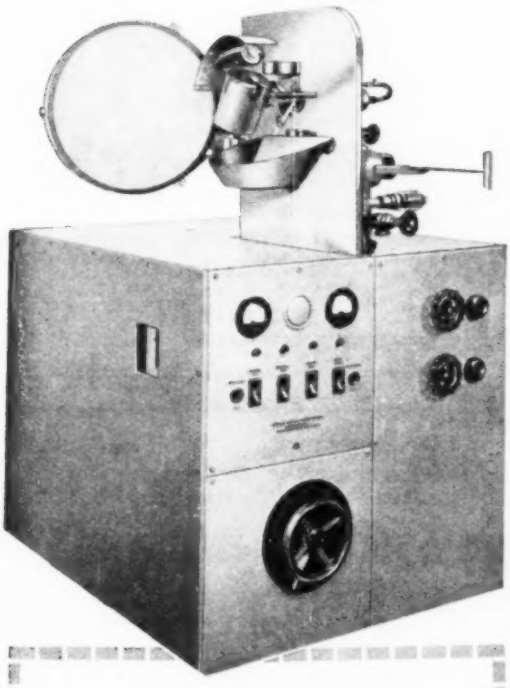

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APPOINTMENTS VACANT

AUSTRALIA
THE UNIVERSITY OF NEW SOUTH WALES
SENIOR LECTURER AND LECTURER IN ANATOMY
FACULTY OF MEDICINE

The University of New South Wales wishes to appoint a Senior Lecturer and a Lecturer to the School of Anatomy, within the Faculty of Medicine.

The successful candidates will be expected to take up their duties in Sydney not later than February, 1962.

Salary:

Senior Lecturer, £A.2,592 range £A.3,042 per annum.
Lecturer, £A.1,772 range £A.2,477 per annum.

Commencing salaries for these positions are determined by qualifications and experience.

Successful applicants will be eligible, subject to passing a medical examination, to contribute to the State Superannuation Fund.

First-class ship fares to Sydney of appointees and their families will be paid.

Details of conditions of appointment, etc., may be obtained from the Agent-General for New South Wales in London.

Four copies of applications (including the names of three referees), should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded by airmail to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, to arrive before July 31, 1961. Applicants outside the United Kingdom and Eire need only send one copy of their application to the London address in addition to that sent to Sydney.

AUSTRALIA
THE UNIVERSITY OF NEW SOUTH WALES
LECTURER IN HISTOLOGY
FACULTY OF MEDICINE

The University of New South Wales wishes to appoint a Lecturer in Histology within the School of Anatomy. The selected applicant will be expected to take up his duties not later than February, 1962.

Salary: £A.1,772 range £A.2,477 per annum.

Commencing salary is determined by qualifications and experience.

Successful applicant will be eligible, subject to passing a medical examination, to contribute to the State Superannuation Fund.

First-class ship fares to Sydney of appointee and his family will be paid.

Details of conditions of appointment, etc., may be obtained from the Agent-General for New South Wales in London.

Four copies of applications (including the names of three referees), should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded by airmail to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, New South Wales, Australia, to arrive before July 31, 1961. Applicants outside the United Kingdom and Eire need only send one copy of their application to the London address in addition to that sent to Sydney.

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RESEARCH CHEMIST

The Organization's **Division of Mineral Chemistry** of the Chemical Research Laboratories at Fishermen's Bend, Melbourne, Victoria, invites applications for appointment as Research Chemist from Honours graduates in Science, majoring in Physical or Inorganic Chemistry or Metallurgy, with some years post-graduate research experience.

The Division conducts research mainly in the field of inorganic chemistry, with particular emphasis on the recovery of valuable materials from minerals and ores. A balance is maintained between work undertaken with specified industrial applications in mind and purely exploratory research from which new materials and uses might emerge. The appointee is required to conduct research in hydrometallurgy, especially at elevated temperatures and will be given considerable freedom in developing his own approach to the investigations. Previous experience in this field is not essential.

SALARY: Dependent on qualifications and experience within the ranges: £A.1,510 to £A.2,265 or £A.2,395 to £A.2,720 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rate for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further particulars of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 601/8) should be addressed by July 8, 1961.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY
MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF MATHEMATICS

Applications are invited for two posts in the Department of Mathematics which may be graded as Senior Lecturer, Lecturer, or Assistant Grade B in accordance with the qualifications of the candidates. Salary scales: (a) Senior Lecturer, £1,550 by £50 to £1,750; Lecturer, £1,370 by £35 to £1,550; (c) Assistant (Grade B), £700 by £27 10s. to £1,150, plus additions for training and graduate status. London allowance of £38 or £51, according to age.

Particulars and form of application from the Clerk to the Governors. Applications to be submitted by June 9, 1961.

UNIVERSITY OF NATAL
DEPARTMENT OF MATHEMATICS AND APPLIED MATHEMATICS

Applications are invited from suitably qualified persons for appointment to the post of Senior Lecturer in Mathematics or Applied Mathematics, Durban. A background in statistics is desirable but not a necessity. The salary scale attached to the post is R.3,180 by R.120 to R.4,140 (£1,590 by £60 to £2,070) per annum.

Application forms and further particulars of the post, including commencing dates, etc., are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in South Africa and London, on June 20, 1961.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH PHYSICIST

The Organization's **Division of Physics,** located in the grounds of Sydney University, N.S.W., invites applications for a position as Physicist from Honours graduates, majoring in Physics (or equivalent qualifications), with considerable post-graduate research experience preferably, though not essentially, in physical optics.

The appointee will be required to undertake fundamental investigations of atmospheric "seeing," or the effect of the atmosphere on optical imagery. The aim is to relate seeing to atmospheric structure, meteorological conditions and terrain. The results of the work, which will be primarily experimental, are of significance in the selection of observatory sites, telescope design, and in a wide range of other optical problems. Facilities include a comprehensive optics laboratory and optical and mechanical workshops.

Salary: Dependent on qualifications and experience within the ranges £A.1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the range within which the original appointment is made.

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Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

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UNIVERSITY OF ABERDEEN

RESEARCH FELLOWSHIP

Applications are invited from honours graduates in chemistry, biochemistry or agricultural chemistry, for a Fellowship to study chemical changes in forest litter in the Department of Soil Science under a grant from the Forestry Commission. The appointment will be from October 1, 1961, normally for three years. Salary on scale £800 by £50 to £900 with F.S.S.U.

Further particulars may be obtained from the Secretary, the University, Aberdeen, to whom applications (three copies), should be sent not later than June 30, 1961.

UNIVERSITY OF BRISTOL

Applications are invited for the post of Assistant Lecturer (Grade III) in Botany. Initial salary within the scale £800 by £50 to £950 per annum with superannuation and family allowance benefits.

Full details may be obtained from the Registrar, University, Bristol 8, to whom applications should be sent by June 17.

UNIVERSITY OF ABERDEEN

DEPARTMENT OF PHYSIOLOGY

Applications are invited for post of Lecturer. Salary if medically qualified on scale £1,050 to £2,100, otherwise on scale £1,050 to £1,850. Superannuation, child allowance, and removal allowance. Appointment from October 1, 1961, or date to be arranged.

Further particulars may be obtained from the Secretary, The University, Aberdeen, with whom applications (eight copies) should be lodged not later than June 18, 1961.

UNIVERSITY COLLEGE LONDON (Gower Street, W.C.1) requires graduate in mechanical engineering or applied mathematics to conduct research on an aspect of vibration concerned with transport. Appointment will be made as soon as possible and, in first instance, will be for period to March, 1964. Salary up to £1,300 per annum.—Applications, to be received by June 24, 1961, should be sent to the Secretary, from whom further particulars may be obtained.

RUBBER RESEARCH INSTITUTE OF MALAYA

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Applications are invited for the post of Deputy Director which will shortly become vacant on the retirement of the present Deputy Director.

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Qualifications:

Applicants, whose age should preferably not exceed 45 years, should be science graduates with considerable research experience and possessing administrative ability. Training and research experience in plant physiology or biochemistry would be particularly suitable.

Duties: To assist the Director with the administration of the Institute, particularly with the preparation of the research programmes, and the co-ordination of the work of the biological divisions, in which connection the stimulation and co-ordination of research in the fields of plant physiology and biochemistry is of special importance.

Terms: Basic salary $2,900 per month ($= 2s. 4d.); in addition the following allowances are payable:

Employee of Malayan domicile: Cost of living allowance $100 per month.

Employee of Overseas domicile: Cost of living allowance $100 per month, overseas allowance $350 per month, additional allowance $100 per month for each child up to a maximum of three children under the age of 18 years is payable. First-class passages are provided for the employee, his wife and children up to a maximum of four first-class fares.

There is a contributory Provident Fund to which the employee contributes 15% of his monthly basic salary and the Board contributes a like amount.

Long leave on full salary at the rate of two months per year of service is normally granted every 18 months.

Rent-free quarters with heavy furniture are provided or an allowance in lieu thereof.

Medical Attention:

Medical attention will be provided by the Board's medical advisers for an employee, his wife and children up to the age of 12 years, but does not include operation charges nor dental treatment unless the latter is on the recommendation of the Board's medical advisers.

Application forms can be obtained from the Secretary, Rubber Research Institute of Malaya, P.O. Box 150, Kuala Lumpur, Malaya, or from the London Representative, Malayan Rubber Fund Board, 19 Buckingham Street, London, W.C.2, from whom further particulars of the appointment are available.

The closing date for receiving applications is July 31, 1961.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for the post of Demonstrator in Organic Chemistry. The Demonstrator would be expected to engage in research work, normally for higher degree. The appointment is tenable from September 1, 1961. Remuneration £620 per annum. The appointment is renewable annually. Usual tenure is for three years.

Applications should reach the Registrar, the College, Keele, Staffs, from whom further particulars and application forms may be obtained, not later than June 14, 1961.

RESEARCH CHEMIST

An opportunity has occurred for a young graduate, preferably of honours degree standard, to participate in the development of new products in the laboratories of an organization near Edinburgh. The work is stimulating and varied, with organic synthesis holding a dominant position in the present programme. The salary paid will be in accordance with qualifications and experience, but in any case will not be less than £720 per annum.

Applications, which will be treated in confidence, should be sent to Box No. 968, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH OFFICER OR SENIOR RESEARCH OFFICER

(NO. 490/98)

The Organization's **Commonwealth Research Station, Merbein** (near Mildura), Victoria, invites applications for a research position from Honours graduates in Science, preferably majoring in Chemistry or Biochemistry (or equivalent qualifications), with several years post-graduate research experience.

The Station undertakes physiological and agronomic studies of the grapevine under irrigation; chemical and physical work on the processing of dried fruits; and basic and practical hydrological work on the movement of water in soils. Work on nematology and plant breeding is also undertaken. The appointee will be required to undertake investigations into the process involved in, and changes taking place in, the drying of grapes which gives scope for fundamental research on chemical, biochemical, physical or microbiological aspects according to his interests. Attention may also be given to interesting problems in the field and factory handling of fruit.

ECOLOGIST

FOR BIOLOGICAL CONTROL STUDIES

(NO. 180/182)

The Organization's **Division of Entomology, Canberra, A.C.T.**, invites applications from Honours graduates in Science (or equivalent qualifications) with some years relevant post-graduate training and/or experience for appointment as entomologist to join the Biological Control Unit.

As part of the Division's extensive programme of studies related to the biological control of insects and weeds and attempts to colonize beneficial introduced insects into Australia, the appointee, who will be stationed initially at Brisbane, will be required to investigate the effect of a cerambycid beetle, *Megacyllene caryinna* to be liberated in Queensland in 1962 against the important weed, Noogoora burr. His general programme will include a study of other candidate insects for control of this and other weed problems. An entomologist is needed who, ideally, is interested not only in biological control but also in the population dynamics and behaviour of insects. A knowledge of ecology is desirable but not essential.

SALARY: Dependent on qualifications and experience within the ranges: £A.1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

RESEARCH CHEMIST OR BIOCHEMIST

(NO. 400/91)

The Organization's **Fodder Conservation Section, Melbourne, Victoria**, invites applications from Honours graduates in Science or Agricultural Science (or equivalent qualifications) with appropriate post-graduate research experience for the position of Research Chemist or Biochemist to participate in an expanded programme of basic research on silage making. Familiarity with chromatographic techniques, preferably including gas-liquid chromatography, is desirable.

Ensilage is one of the most important methods of conserving fodder in Australia, particularly to the dairy industry. Serious difficulties are associated with the ensiling of high protein pastures and present methods result in heavy losses of nutrient materials. The appointee will join a team investigating various aspects of this process including chemical changes leading to such losses. Volatile products of bacterial metabolism such as fatty acids and nitrogenous compounds appear worth special attention.

SALARY: Dependent on qualifications and experience within the range: £A.1,510 to £A.2,265 per annum.

By arrangement with the successful candidate, this appointment may either be permanent or for a fixed term of three years.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Salary for women will be £A.180 per annum less than corresponding rates for men.

Fares paid and, in the case of a short-term contract, return fares will also be paid.

Further particulars on conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting relevant Appointment number) should be addressed by July 8, 1961.

TULLIS RUSSELL & CO. LTD., REQUIRE the services of a Laboratory Manager. Qualifications should include a good degree in science and considerable experience of laboratory organization, preferably but not necessarily, in the paper industry.—Applications to the Chief Chemist, Tullis Russell & Co. Ltd., Auchmuty & Rothes Paper Mills, Markinch, Fife.

THE BRITISH DRUG HOUSES LTD. HAVE a vacancy for a young honours graduate to work in their Research Department in the steroid field. The Company offers good conditions of employment.—Write, with full details of age, qualifications and salary required, to: Ref. HAC/VP, Personnel Manager, The British Drug Houses Ltd., Graham Street, London, N.1.

GLACIER METAL CO. LTD.
KIRKSTYLE, KILMARNOCK, AYRSHIRE

invite applications for the position of

RESEARCH ENGINEER

A Research Engineer is required for the Metallurgy Department of the Research and Development Organization to work on the problem of fatigue failure in engine bearing materials.

The work involves the mathematical analysis of the stresses in engine bearings and the development of longer fatigue life bearing materials. Test rigs simulating engine bearing conditions and other facilities will be available.

Applicants should have a degree in engineering or metallurgy and a flair for research. A strong interest in and a capacity for mathematical techniques are essential.

Starting salary will depend on qualifications and experience but will probably be within the range £1,100 to £1,400 per annum.

Brief details of age, qualifications, experience and present salary should be sent to Personnel Department, quoting reference No. 3/RDO/6/61/NA.

UNIVERSITY OF QUEENSLAND

LECTURER IN ZOOLOGY

Applications are invited for the above-mentioned position. Applicants should have a science degree with zoology as a major subject, followed by postgraduate experience leading to a higher degree and/or to published work. An applicant should indicate his general sphere of competence and also his especial interests.

Salary £A.1,830 to £A.2,330 per annum.

The successful applicant will enjoy the privileges of superannuation, study leave, travel grants and other benefits available to the academic staff.

Further particulars and application forms are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1.

Applications close, in Australia and London, on June 30, 1961.

UNIVERSITY OF MELBOURNE

TWO CHAIRS IN CHEMISTRY

Applications are invited for two Chairs in the School of Chemistry—(1) a Chair of Organic Chemistry and (2) a Chair of Chemistry. For the Chair of Chemistry preference will be given to an inorganic chemist. There is also a Chair of Physical Chemistry which is at present occupied. One of the three Professors will be designated Head of the School. The salary for each Chair is £A.4,000 per annum, and the Head of the School will receive a loading of £A.450. It is expected that an upward revision of £A.250 will shortly take place. Superannuation similar to F.S.S.U. in Great Britain will be provided.

Further particulars and conditions of appointment may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on July 31, 1961.

UNIVERSITY OF WESTERN AUSTRALIA

READERSHIP IN MATHEMATICS

Applications are invited for appointment to the above-named position in the Department of Mathematics. The Department is responsible for teaching and research in pure mathematics, applied mathematics and mathematical statistics and the appointee may be a specialist in any branch of these three fields of mathematics. The salary range for the position is £A.3,010 by £A.60 to £A.3,250 per annum, with superannuation similar to F.S.S.U.

It is important that intending applicants obtain details of the procedure to be followed in applying for the post and a copy of the Conditions of Appointment before submitting their applications. This information is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on July 31, 1961.

UNIVERSITY OF AUCKLAND
NEW ZEALAND
SENIOR LECTURESHIP AND LECTURESHIP IN NUCLEAR PHYSICS

Applications are invited for the above-mentioned posts. The Department is interested in various research fields, including angular correlation of nuclear radiations; polarized nuclear reactions; ion optics; time-of-flight neutrons. Preference would be given, other things being equal, to candidates with theoretical or experimental knowledge of any of the above fields or similar fields. The Department has a 600 KeV. Cockcroft-Walton accelerator, which will later be supplemented by a Van de Graaf accelerator (2-2.5 MeV.), at present being shipped out from the United Kingdom. There are very good and rapidly increasing facilities and opportunities for experimental or theoretical nuclear research. The salary scale for a Senior Lecturer is £1,750 per annum, rising to £2,000, and for a Lecturer, £1,250 per annum, rising to £1,700. Commencing salaries within these scales will be determined according to qualifications and experience. Approved fares to New Zealand will be allowed for an appointee, his wife and children, and there is a generous allowance for baggage.

Further particulars and information as to the method of application, together with details of Superannuation and Study Leave Schemes, should be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in New Zealand and London, on July 15, 1961.

THE POLYTECHNIC
309 REGENT STREET, W.1
SCHOOL OF COMMERCE

Applications are invited for a full-time appointment as Lecturer to teach Mathematics and Mathematical Statistics to Institute of Statisticians and Economics degree finals standard. Candidates should possess a good honours degree (1) in mathematics and be interested in mathematical statistics, or (2) in economics with statistics. Duties to commence on September 1 next, or January 1, 1962. The salary scale commences at £1,170 and rises to £1,550 per annum, plus London allowance of £38 or £51. The post is subject to superannuation and some concession in this respect may be made for previous industrial employment.

Application form, to be returned by June 17, may be obtained by sending a stamped addressed foolscap envelope to the undersigned.

J. E. RICHARDSON,
Director of Education.

BRISTOL COLLEGE OF SCIENCE AND TECHNOLOGY
ASHLEY DOWN, BRISTOL, 7

The Governors invite applications from graduates and others holding an equivalent professional qualification, together with industrial, research or teaching experience, for the post of Lecturer in Microbiology. Experience in either food bacteriology or bacterial physiology is essential. The person appointed will be required to teach at Diploma in Technology and professional qualification level; an active personal interest in research is essential. Salary within range £1,370 to £1,550. Scale at present under review.

Application forms and details from the Registrar. Please quote ref. CST 61/12.

ROYAL MILITARY COLLEGE OF Science, Shrivenham, Berkshire, require Senior Lecturers or Lecturers in Physics, Mathematics and Electrical Engineering. Teaching at university level. To lecture to degree courses (and possibly specialized courses) and assist with laboratory classes. There are extensive well-equipped laboratories. Research encouraged and work would be suitable for publication and submission for higher degree. Qualifications: First- or second-class honours degree or equivalent, preferably with teaching and/or research experience. Physicist expected to engage in research in nuclear physics, radiation physics or solid state physics. Mathematician should preferably have interest in applied mathematics. Electrical Engineer to have thorough grounding in electrical engineering, experience in electrical power and machines and/or electrical theory and measurements. Salary range: Senior Lecturer, £1,302 to £1,604; Lecturer, £717 to £1,186. Starting pay may be above minimum in both cases: credit for postgraduate experience and National Service. Superannuation under F.S.S.U. Good prospects of permanency. Residential accommodation for single staff, houses for married staff.—Further particulars and forms from Registrar, R.M.C.S., Shrivenham, Berks, quoting reference H.Q.77/17.

AUSTRALIA
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

EXPERIMENTAL OFFICER—ORCHARD INVESTIGATIONS

The Organization's **Division of Entomology, Canberra, A.C.T.**, invites applications for the position of Experimental Officer—Orchard Investigations from graduates in Science or Agricultural Science, preferably majoring in Entomology, or with training to full professional status in Horticulture. Experience in horticulture, preferably in pomology, an advantage.

The Orchards Investigations Section is engaged in long-term population studies of orchard arthropods with a view to developing measures of plant protection fully consistent with the economy of the pest species (Pest Management). Particular attention is currently being given to codling moth and related species on pome fruits involving observations and experiments in the field and the laboratory. Investigations will later be extended to other pests and other types of fruits. The appointee will assist in planning, organizing, implementing and supervising ecological research work and in interpreting numerical results.

SALARY: Dependent on qualifications and experience within the ranges: £A1,070 to £A1,620 per annum or £A1,620 to £A1,950 per annum.

Salary for a woman will be £A180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the scale within which the original appointment is made.

Fares paid. Further particulars of conditions, etc., supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting Appointment No. 180/1691 should be addressed by July 31, 1961.

Ferranti electronics

invite applications from

ELECTRONIC ENGINEERS AND PHYSICISTS

for development work on diverse problems of a fundamental nature including

(1) THIN MAGNETIC FILM STORES FOR COMPUTERS

(2) FIBRE OPTICS

(3) TRANSPARENT PHOSPHOR AND VAPOUR PHASE STUDIES

(4) SPECIALISED CATHODE-RAY TUBES

Applicants should possess a degree or H.N.C. in Electrical Engineering or Physics, and for the first-named topic should have had experience of research and development in this field. The vacancies clearly offer the opportunity of varied experience in interesting branches of Applied Physics and carry attractive salaries which are subject to annual review.

Application forms can be obtained from T. J. Lunt, Staff Manager, Ferranti Limited, Hollinwood, Lancs. Please quote reference GCT.

ENGLISH ELECTRIC VALVE CO. LTD.

Chelmsford, Essex

The Company has in production high quality germanium and silicon power rectifiers in ratings up to 20 amps.

Improvement in the processes involved in the manufacture of these devices continues in order to increase their reliability in service.

The Company wishes to engage a senior production-development engineer to accept responsibility in the development and production of the rectifiers in current demand, and other devices that the Company wish to market after development.

A substantial salary will be paid to an engineer or physicist possessing sound experience in the semi-conductor field and post-graduate qualifications. Preferred age range 28 to 40.

Applications outlining experience and qualifications should be sent to: Group Personnel Services, English Electric House, Strand, London, W.C.2. Please quote reference N.1594.K.

THE EDINBURGH AND EAST OF SCOTland College of Agriculture invite applications for post of Beekeeping adviser in the Extension Service of the College. Applicants must possess a very wide practical and technical knowledge of the subject, and have experience in teaching and advisory work. Salary: Grade III (£1,004 to £1,570) or Grade A (£1,061 to £1,290), depending upon qualifications and experience.—Particulars and application form obtainable from Secretary, School of Agriculture, West Mains Road, Edinburgh, with whom application should be lodged not later than June 30, 1961.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Research Assistant required for clinical isotope unit of Radiotherapy Department in the Royal Marsden Hospital, Fulham Road, S.W.3. Previous laboratory experience in clinical pathology, or chemistry, or with isotopes, desirable. Candidates with A.I.M.L.T. Higher National Certificate or equivalent qualification preferred. Salary according to age, qualifications and experience in range £410 to £860.—Apply, with names of two referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref. 301/B/66.

AUSTRALIAN NATIONAL UNIVERSITY

INSTITUTE OF ADVANCED STUDIES
JOHN CURTIN SCHOOL OF MEDICAL RESEARCH
RESEARCH FELLOWSHIP IN PHYSICAL BIOCHEMISTRY

Applications are invited for a Research Fellowship in the Department of Physical Biochemistry.

Research experience in biochemistry or chemistry and interest in physico-chemical aspects of biochemistry are essential. The Research Fellow will be allowed reasonable scope in the choice of his research.

The salary range for Research Fellows is £A.1,625 to £A.2,450, with increments of £A.75 per annum; initial salary will depend on qualifications and experience. Appointment is for three years, with possible extension to a maximum of five years.

Superannuation is on the F.S.S.U. pattern. Reasonable travel expenses are paid and assistance with housing is provided.

A summary of the conditions of appointment is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1.

Applications close in Australia and London on June 30, 1961.

Details of the research being carried out may be obtained from the Head of the Department, Professor A. G. Ogston, F.R.S.

UNIVERSITY COLLEGE

IBADAN, NIGERIA

Applications are invited for post of Photocopy Technician to supervise University Library microfilm and photocopying section. Laboratory and practical experience required; appropriate examination qualifications an advantage. Thorough knowledge of processes of documentary reproduction essential. Appointment to commence October, 1961, if possible. Salary scales: Senior Technician, £1,050 by £25 to £1,100 (bar); £1,150 by £50 to £1,400 per annum. Technician, £950 by £25 to £1,050 per annum. Passages paid for appointee, wife and up to five children under 11 years on appointment, annual overseas leave and termination. Part-furnished accommodation at rent not exceeding 7½ per cent of salary. Children's, car and outfit allowances. Pension Scheme.

Detailed applications (six copies), naming three referees, by July 5, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

SK&F

wish to appoint

a

BIOCHEMIST

in their

PHARMACOLOGY DEPARTMENT

The post is newly created and the successful applicant will be responsible for the control of all biochemical investigations within the department.

He will be particularly concerned with studies of the actions of new synthetic drugs on metabolic processes with a view to elucidating their mechanisms of action and developing new screening methods for pharmacological activity.

Participation in meetings of scientific societies and publication of results are encouraged.

Previous research experience is essential and the preferred age range is 25-35 years.

An attractive starting salary with annual merit reviews is offered and congenial working conditions in new and well equipped laboratories will be provided.

Other Company benefits include a non-contributory Pension and Life Assurance Scheme, Staff Cafeteria and an active Sports and Social Club.

Under certain circumstances a married man may be eligible for rented unfurnished accommodation and full payment of removal expenses will be made.

Letters of application, giving fullest possible details considered relevant, should be addressed to:

SK&F

The Staff Manager,
SMITH KLINE & FRENCH LABORATORIES LTD.,
Mundells, Welwyn Garden City, Herts.

Please quote Reference No. L.1473.

NEW ZEALAND METEOROLOGICAL SERVICE

AIR DEPARTMENT

VACANCIES FOR UNIVERSITY GRADUATES

The New Zealand Meteorological Service has immediate vacancies for suitable university graduates wishing to follow professional meteorology as a career in New Zealand.

Qualifications: For preference, applicants should possess a B.Sc. Special degree in Mathematics and/or Physics, but consideration would be given to those with B.Sc. General. Students expecting to complete their degree this year are eligible to apply.

Training: For those without previous experience professional meteorological training will be given in Wellington, New Zealand.

Duties: Appointees, after training, will be engaged on professional meteorological work as considered most appropriate to their individual aptitudes. In general, they will do weather analysis and forecasting, but opportunities are given for concurrent investigational work. In addition, there are interesting openings for suitable specialized officers in research, climatology, aericultural meteorology, instruments, hydrology, etc.

Salary: Minimum starting salaries for appointees with no previous experience are:

B.Sc. General	£445 per annum
B.Sc. Special	£805 „ „
B.Sc. Special — Second-class honours	£850 „ „
B.Sc. Special — First-class Honours	£900 „ „
Higher qualifications	as applicable

In determination of actual starting salary, credit may be given for any postgraduate scientific work or study. Officers of average ability may rise to £1,700 per annum, and those with exceptional ability to a maximum of £2,300. Salary payments start on taking up duty in New Zealand.

Locations: Initial location for training will be Wellington, New Zealand. Thereafter, officers may serve at one of the forecasting branch offices either in New Zealand or Fiji.

Passages: Steamer fares of up to £172 each for the appointee and his wife, and pro rata for dependent children will be paid.

Incidental Expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and further details are available from the High Commissioner for New Zealand, 415 Strand, London, W.C.2, with whom applications will close on June 22, 1961.

Please quote reference B13/3/1 when inquiring.

UNIVERSITY OF OXFORD

INSTITUTE OF EXPERIMENTAL PSYCHOLOGY

There are two vacancies for research on brain stem stimulation and behaviour in pigeons. (1) Scientific Assistant. Preferably at post-doctoral level, but more junior applicants will be considered. Salary at post-doctoral level £1,000 by £50 to £1,200; lower level in accordance with qualifications. Preference given to applicants with experience in animal behaviour or neurophysiology. (2) Research Studentship. For work on brain stimulation or recording in pigeons, with particular reference to instinctive behaviour patterns. Salary £450 per annum, plus approved College and University fees.

Further information on these two posts can be obtained from Dr. D. M. Vowles, Institute of Experimental Psychology, 1 South Parks Road, Oxford, to whom application should be made not later than June 20, 1961.

SULLY HOSPITAL

SULLY, PENARTH, GLAM

Senior Biochemist required. The hospital is Regional Thoracic Centre for treatment of all thoracic, including cardio-vascular conditions, in adults and children, and has full pathology, surgical and medical facilities with cardio-respiratory laboratory and animal research laboratory. Work will include co-operation with surgical colleagues in research projects, and individual research will also be encouraged. N.H.S. conditions and salary (£1,250 to £1,700 per annum). Applicants should hold appropriate science degree of university of England, Wales, Scotland or Ireland or Associateship or Graduate Membership of the Royal Institute of Chemistry or such other qualification as may be approved for the purpose by the Minister of Health.

Form of application from Group Secretary, 44 Cathedral Road, Cardiff.

EMI

INORGANIC CHEMIST

The Solid State section of the E.M.I. Research Laboratories have a vacancy for a young chemist to carry out research studies of the preparation and structural properties of iron oxides and related materials used in the manufacture of magnetic recording tape.

Applications are invited from first- or second-class Honours Graduates, preferably with one or two years industrial experience not necessarily in this field, who have an interest in inorganic chemistry.

A good starting salary is offered and the post affords ample opportunity for progress.

Please write, quoting ref. RES 2, to:

Personnel Manager,
E.M.I. Limited,
Blyth Road,
Hayes, Middlesex.

BEECHAM GROUP

RESEARCH SCIENTIST

An opportunity with excellent prospects is being created by expansion activity in nutritional research.

A seasoned graduate (first- or second-class honours) is sought with experience in one or more of the following fields:

Biochemistry.
Food Chemistry.
Nutrition.

A postgraduate qualification is desirable, but appropriate experience would be an equivalent asset.

The successful applicant would work in the Basic Research Unit at Brentford, and be directly responsible to the Manager of the Unit. Prospects are excellent for the right man.

Applications, giving full details of age, qualifications and experience, and quoting reference RS 132, should be addressed to the Personnel Director, Beecham Group Limited, Beecham House, Great West Road, Brentford, Middlesex.

UNIVERSITY OF WESTERN AUSTRALIA

LECTURESHIP IN MATHEMATICS

Applications are invited for appointment to the above-named position in the Department of Mathematics. The Department is responsible for teaching and research in pure mathematics, applied mathematics and mathematical statistics and the appointee may be a specialist in any branch of these three fields of mathematics. The salary range for the position is £A.1,750 by £A.75 to £A.2,350 per annum with superannuation similar to F.S.S.U.

It is important that intending applicants obtain details of the procedure to be followed in applying for the post and a copy of the Conditions of Appointment, before submitting their applications. This information is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on July 31, 1961.

UNIVERSITY OF ST. ANDREWS

Applications are invited for a Lectureship in Pharmacology in the Department of Pharmacology and Therapeutics, Queen's College, Dundee, with effect from a date to be arranged. Salary scale: medically qualified, £1,050 by £100 to £2,000 (efficiency bar £1,450); non-medically qualified, £1,050 by £50 to £1,400 (efficiency bar) by £75 to £1,850. Placing on appropriate scale according to qualifications and experience, but at a stage below the efficiency bar. Preference will be given to applicants possessing postgraduate science degrees in Pharmacology. F.S.S.U. Family allowance. Grant towards furniture removal expenses.

Applications (six copies), containing the names of three referees, to the undernoted not later than June 24, 1961.

PATRICK CUMMING,
Joint Clerk to the University Court.
Queen's College, Dundee.

UNIVERSITY OF SOUTHAMPTON

Applications are invited for the post of Lecturer or Assistant Lecturer in Civil Engineering. New Departmental laboratories are to be occupied shortly which will offer very good facilities for research in all fields of Civil Engineering. Salary scales: Lecturer, £1,050 by £50 to £1,400 by £75 to £1,850 with an efficiency bar at £1,475; Assistant Lecturer, £800 by £50 to £950. The initial salary will depend on qualifications and experience.

Further particulars should be obtained from the Secretary and Registrar, the University, Southampton, to whom applications (seven copies from United Kingdom applicants) should be sent not later than June 30, 1961.

JOHN INNES INSTITUTE REQUIRE A Scientific Officer or Senior Scientific Officer to work on biochemical aspects of genetics. The successful applicant will be expected, in the first instance, to assist in current research on the effects of mutation on the structure of specific proteins in the mould *Neurospora crassa* but there will also be scope for the development of individual lines of research. Applicants should have research experience in enzymology and/or protein chemistry, and some knowledge of and interest in fundamental genetic problems. Salary in the scale £750 to £1,342 per annum, according to age and qualifications. F.S.S.U.

Applications, with the names of two referees, should reach the Secretary, Bayfordbury, Hertford, Herts, by June 30, 1961.

NEW ZEALAND
EDUCATION DEPARTMENT

Applications are invited for the undermentioned vacancy: Inspector of Post-Primary Schools (Technical), Head Office, Department of Education, Wellington, New Zealand. Duties: To assist the Superintendent of Technical Education in the development of Senior Technical education. Location: The appointee will be attached to Head Office, Wellington, but may be required to travel anywhere in New Zealand. Salary: The salary range for the position is from £1,600 to £1,900 per annum. Commencing salary will depend on experience and qualifications of the applicant, and is payable from the day of taking up duty in New Zealand. Qualifications: Applicants should be well qualified in chemistry or one of the biological sciences, and should, if possible, have had industrial as well as teaching experience. Conditions: The successful applicant will be expected to take up duties in New Zealand as soon as possible. Passages: Steamer fares of up to £172 each for the appointee and his wife, and pro rata for dependent children will be paid. Incidental Expenses: Up to £35 for a single person and £100 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and further details are available from the High Commissioner for New Zealand, 415 Strand, London, W.C.2, with whom applications will close on June 26, 1961. Please quote reference B13/6/1 when inquiring.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY
(FACULTY OF TECHNOLOGY IN THE UNIVERSITY OF MANCHESTER)
APPOINTMENT OF LECTURER IN METALLURGY

Applications are invited for the post of Lecturer in Metallurgy with the title and status of Lecturer in the University of Manchester. Salary according to qualifications in the scale £1,050 to £1,850. Superannuation under the F.S.S.U. Family allowances. Candidates must be prepared to undertake or supervise research for which there are excellent facilities.

Conditions of appointment and application form may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester 1, to whom applications must be returned by Saturday, June 24, 1961.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY
(FACULTY OF TECHNOLOGY IN THE UNIVERSITY OF MANCHESTER)

Applications are invited for a Research Award, valued at £900 to £1,000 per annum and tenable in the Department of Chemistry, designed to enable an experienced, and preferably post-doctoral, research chemist to work on a problem on heterogeneous catalysis as applied to polymerization, under the general direction of Dr. H. Steiner.

Applications should be addressed to the Registrar of the College, Sackville Street, Manchester 1, as soon as possible.

UNIVERSITY OF DUBLIN
TRINITY COLLEGE
SCHOOL OF VETERINARY MEDICINE
LECTURER IN VETERINARY ANATOMY

Applications are invited from suitably qualified persons for the post of Lecturer in Veterinary Anatomy; duties to be taken up as soon as possible. Salary in the range £1,045 by £47 10s. to £1,377 10s. by £23 15s. to £1,520 per annum, with membership of a non-contributory superannuation and life assurance scheme, and with marriage and child allowances. £75 of the salary is regarded as expenses.

Applications (four copies), giving full details of career and experience, and the names and addresses of three referees, should reach the Registrar, Trinity College, Dublin 2, from whom further particulars may be obtained, not later than June 26, 1961.

DURHAM COLLEGES
IN THE UNIVERSITY OF DURHAM

Applications are invited from graduates, preferably women, for the post of Map Assistant in the Department of Geography. Salary £600 to £700, according to qualifications. Appointment is for one year in the first instance, from September 1, 1961.

Applications (three copies), together with the names of two referees, should be sent not later than June 30 to the Secretary, 38 North Bailey, Durham, from whom further particulars may be obtained.

NORTH LINDSEY TECHNICAL COLLEGE
KINGSWAY, SCUNTHORPE, LINCS.
Principal: F. C. Jones, B.Sc.(Eng.), A.M.I.Mech.E., A.M.I.E.E.
DEPARTMENT OF SCIENCE AND METALLURGY

Applications are invited for the post of Assistant Lecturer Grade B to teach Physics and Mathematics mainly to Ordinary National Certificate classes, duties to commence on September 1, 1961. A university degree or equivalent qualifications are desirable. The vacancy is created by the resignation of the present teacher to take up a higher appointment. The salary is in accordance with the Burnham Scale for Teachers in Technical Colleges, Assistant Grade B, £700 to £1,150 per annum with the usual allowances for qualifications and experience. To a suitable candidate an allowance of £120 per annum for special responsibility may be allocated.

Forms of application and further particulars may be obtained from the Principal at the above address, to whom completed applications should be returned by June 10, 1961.

JENSON & NICHOLSON LTD.

require a

SENIOR CHEMIST

FOR THEIR WOOD FINISHES DEVELOPMENT LABORATORY

with wide experience in the field of development and application of modern wood finishes, both clear and pigmented, including polyesters, polyurethanes, nitrocellulose and acid catalysed materials. Familiarity with electrostatic and curtain coating methods and with current practice in industry is essential. Salary commensurate with the wide experience required.

Applications, giving details of age, qualifications, experience and appointments held, quoting Ref. B.100, should be addressed to the **Personnel Manager, Jenson & Nicholson Ltd., Carpenters Road, Stratford, London E.15.**

CITY OF PORTSMOUTH COLLEGE OF TECHNOLOGY
DEPARTMENT OF MATHEMATICS AND PHYSICS
RESEARCH ASSISTANT

Applications are invited for the post of Research Assistant. The person appointed will be expected to take part in research work on the microwave properties of certain magnetic oxides and to undertake a certain amount of teaching. The appointment is for three years, and is intended to enable a candidate to prepare for a higher degree. Salary is in the range £650 to £700.

Further particulars and a form of application, which should be returned by June 17, may be obtained from the Registrar, College of Technology, Park Road, Portsmouth.

APPLICATIONS ARE INVITED FOR THE position of Assistant Professor of Biology with specialization in Limnobiology. Ph.D. standing or its equivalent from a recognized University is essential. Salary will be in the range $7,000 to $8,500, depending upon qualifications and experience. Appointment dates from July 1, 1962. Duties at the University commence not later than September 1, 1962, and include undergraduate teaching in general biology and a programme of research and graduate teaching in Limnobiology. Facilities in this field are excellent.—Applications, including curriculum vitae, names of referees, and a recent photograph, should be addressed to Head of Department of Biology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.

DURHAM COLLEGES
IN THE UNIVERSITY OF DURHAM

Applications are invited for the post of Research Assistant in Geography, with special interests in climatology and meteorology, and ecology or physical geography. The appointment, to date from October 1, 1961, will be for three years. Salary in the range £650 to £900 a year, with F.S.S.U.

Applications (three copies), together with the names of three referees, should be sent not later than June 30, 1961, to the Secretary, 38 North Bailey, Durham, from whom further details may be obtained.

BRITISH EMPIRE CANCER CAMPAIGN

A Graduate Electrical or Electronics Engineer, age about 25 to 30, is required to collaborate in the development and experimental use of an electron linear accelerator, 3 cm. microwave spectroscope, and other experimental equipment which is being used to study the chemical and biological effects of microsecond pulses of radiation. Salary in accordance with qualifications and experience.

Apply in writing to the Director, Research Unit in Radiobiology, Mount Vernon Hospital, Northwood, Middlesex.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

A vacancy exists in the Chemical Engineering Department for a graduate with good first degree in chemistry, physics or chemical engineering to undertake research for a higher degree on some aspects of flame propagation. £500 to £600 per annum.

Further details from Dr. J. H. Burgoyne, Chemical Engineering Dept., Imperial College, London, S.W.7.

UNIVERSITY OF DURHAM
KING'S COLLEGE
NEWCASTLE UPON TYNE, 1

The Council of King's College invite applications for a Lectureship in the Department of Chemistry; the Lecturer will be associated with the newly appointed Professor of Inorganic Chemistry. The commencing salary will be determined at an appropriate point on the Lecturers' scale (£1,050 to £1,850) according to the age, qualifications and experience of the successful applicant. F.S.S.U. and Child Allowance.

Further particulars may be obtained from the Registrar and Secretary of King's College, to whom applications, together with the names and addresses of three persons to whom reference may be made, should be addressed so as to reach him not later than June 17, 1961.

ESSEX
SOUTH-EAST ESSEX TECHNICAL COLLEGE
LONGBRIDGE ROAD, DAGENHAM

Required September, if possible. Two Lecturers in Chemistry to specialize in Inorganic or Physical Chemistry and teach to Grad.R.I.C. and B.Sc. General Standard. A good honours degree (or equivalent) essential with appropriate teaching experience. Industrial experience and/or postgraduate research desirable. Salaries: £1,370 by £25 (4) by £40 (1) to £1,550 per annum plus London allowance £38 or £51.

Details and application forms from the Clerk to the Governors.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)

Assistant Experimental Officer required in Physics Department to assist in studies of physical properties of dairy products—butter and cheese, etc. He will also be required to construct and modify experimenal testing equipment in the department workshop, and skill in using a lathe would be advantageous. Candidates should possess H.N.C. or pass degree, or, if under 22, G.C.E. "A" level or equivalent. Starting salary within range £450 10s. (at 18) to £776 (at 26) in scale to £983; pension scheme.

Apply, naming two referees to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/4.

GRADUATE IN PHYSICS (OR POSSIBLY Electrical Engineering) required in the Research Deparment of C.A.V. Ltd., to tackle a wide variety of problems. Experience of X-ray diffraction techniques primarily as applied to the metallurgical field will be an advantage, but the main requirement is that the applicant should be versatile and able to devise and construct equipment as necessary.—Write to Staff Employment Officer, C.A.V. Limited, Acton, W.3, quoting Ref. F

RESEARCH CHEMIST

required to work in London on problems connected with drug synthesis. Must be well qualified and have research experience. Pharmaceutical qualifications and background an advantage.

Apply with full particulars to Professor E. E. Turner, F.R.S., Director of Research, Biorex Laboratories Ltd., 47/51 Exmouth Market, E.C.1, marking envelope "Research Chemist."

TECHNICIAN

FOR

RESEARCH ON REINFORCED PLASTER MODEL STRUCTURES

A Technician is required to undertake the construction and testing of structural models under limited supervision. He should hold a H.N.C. or equivalent qualification in a scientific subject, but previous engineering experience is not essential. He must be accustomed to handling and developing testing apparatus and to accurate recording and reduction of observations. The appointment is for two years in the first instance at a salary of £895 to £1,015 per annum. It offers valuable experience in a developing field of engineering science.

Written applications should be sent to Dr. G. Brock, Department of Civil Engineering, The University, Edgbaston, Birmingham, 15.

MARINE BIOLOGY STATION

UNIVERSITY COLLEGE OF NORTH WALES

There is a vacancy for a Photographic Technician at the Marine Biology Station. The salary scale is £490 by £20 to £550 (efficiency bar) to £600 by £25 to £675, the commencing salary being fixed according to qualifications and experience. There is a pension scheme. Applicants should have good qualifications, such as A.I.B.P., and be competent to undertake processing, copying, macro and microphotography and cinematography.

Applications, giving details of experience, together with the names of two referees, should be sent to the Registrar, University College of North Wales, Bangor, to reach him in fourteen days' time.

AUSTRALIA

UNIVERSITY OF NEW SOUTH WALES

The University wishes to appoint Senior Lecturers and Lecturers in the following Faculty:

FACULTY OF SCIENCE

Applied psychology (psychometrics and experimental psychology). Botany. Mathematics. Physics.

Salary: Senior Lecturer, £A.2,586 range £A.3,036 per annum; Lecturer, £A.1,766 range £A.2,471 per annum. Commencing salary is determined by qualifications and experience. Subject to passing medical examination appointees will be eligible to contribute to the State Superannuation Fund. First-class ship fares to Sydney of appointees and family will be paid.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, England, and a copy forwarded to the Appointments Section, The University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Marked SAL.

UNIVERSITY OF ABERDEEN

DEPARTMENT OF BOTANY

Graduate Research Assistant required to study the fine structure of the phloem. Appointment is to be made for a period of three years under terms of a grant made to Professor P. F. Weatherley by D.S.I.R. Experience in study of intra-cellular structure desirable. Salary £850 to £900 to £950 with F.S.S.U. and travelling allowance.

Applications should be sent by June 23, to the Secretary, the University, Aberdeen, from whom further particulars can be obtained.

SENIOR PHYSICIST REQUIRED IN RADIOtherapy Department. Applicants must be graduates in physics, preferably with honours, and should normally have had five years' experience of hospital physics or with radioelements. The post offers development work on physical and instrumental problems. Salary £1,250 per annum rising to £1,700, plus £50 London weighting allowance.—Applications, stating age, experience, qualifications and names of two referees, to the Secretary, Lambeth Hospital, Brook Drive, S.E.11, as soon as possible.

UNIVERSITY OF GLASGOW

LECTURESHIP IN BIOCHEMISTRY

Applications are invited for a Lectureship in Biochemistry. Salary scale: with a medical qualification, £1,050 to £1,900 per annum; without a medical qualification, £1,050 to £1,850 per annum. Initial salary according to experience and qualifications. F.S.S.U. and family allowance benefits.

Applications (eight copies) should be lodged, not later than June 16, 1961, with the undersigned, from whom further particulars may be obtained.

ROBT. T. HUTCHESON,
Secretary of University Court.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

VACANCIES IN POLYMER RESEARCH

Two graduates, preferably with some research experience, required to work with Dr. M. Gordon on the physical chemistry of polymers. One is a more senior post (possibly post-doctoral) for work in the field of the statistics and physical effects of cross-linking. Both researches could afford suitable material for submission for a higher degree.

Apply in writing, giving full academic background and the names of two referees, to Dr. M. Gordon, Chemistry Department, Imperial College, S.W.7.

GENETICIST

required by

AN FORAS TALÚNTAIS (The Agricultural Institute) for applied plant genetics unit within its Plant Sciences Division. Appointment will be to Senior Research Officer or Research Officer grade. Marriage and children's allowances. Superannuation Scheme. ESSENTIAL—Honours Degree in Agriculture, Science or Mathematics. DESIRABLE — Research experience in genetics or cytology.

Further particulars and application forms from Director, An Foras Talúntais, 33, Merrion Road, Dublin 4. Latest date for receipt of completed forms—June 20, 1961.

A.R.C. ANIMAL BREEDING RESEARCH ORGANIZATION

Veterinary Surgeon wanted to assist in clinical and experimental investigations of problems of reproduction in farm animals; previous specialist experience not expected. Applications invited particularly from recent or intending graduates. The appointment will be for three years, and payment will be in the Scientific Officer salary scale (£738 to £1,222), according to qualifications and experience. Superannuation F.S.S.U.

Applications should reach the Secretary, 6 South Oswald Road, Edinburgh, 9, not later than July 31, 1961. Further information available on request.

UNIVERSITY OF BIRMINGHAM

FACULTY OF MEDICINE

Applications are invited for the post of Lecturer (non-medical) in Neuropharmacology, in the Department of Experimental Psychiatry, from October 1, 1961, to carry out research into the actions of drugs on the central nervous system and participate in pre-clinical teaching. Salary within scale £1,050 by £50 to £1,400 by £75 to £1,550; £1,550 by £75 to £1,850, with F.S.S.U. and family allowance benefits.

Applications (six copies), naming three referees, should be sent by June 24, 1961, to the Assistant Registrar, The Medical School, Birmingham, 15, from whom further particulars can be obtained.

APPLICATIONS ARE INVITED FOR A post as Professor of Organic Chemistry which has been created because of the continued expansion of the Department. Minimum salary $12,000 per annum. Candidates should send their applications (which should include the names of three referees) immediately to Professor C. A. McDowell, Department of Chemistry, University of British Columbia, Vancouver 8, B.C., Canada, from whom further particulars may be obtained.—Interviews may be arranged in London between June 26 and July 25, 1961, by writing to Professor C. A. McDowell, c/o British Columbia House, Regent Street, London, W.1, during the above period.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

(AMENDED ADVERTISEMENT)

Applications are invited for the post of Demonstrator in Biology Department. Candidates should have a good honours degree in biology or zoology, and preference will be given to those with experience in practical genetics. Salary £620 per annum.

Application forms and further particulars can be obtained from the Registrar, The College, Keele, Staffs, to whom completed forms should be returned not later than June 15, 1961.

BOROUGH POLYTECHNIC

BOROUGH ROAD, S.E.1

A Research Technician is required for work in the Department of Chemistry and Food Technology on chemical and fermentation studies of the cocoa bean. Candidates, including non-graduates, should have had some experience in a biochemical research laboratory. Facilities for part-time study will be available. Salary according to qualifications and experience.

Applications should be forwarded to the Secretary, Borough Polytechnic, Borough Road, London, S.E.1.

TECHNICIAN (FEMALE) REQUIRED FOR new expanding Physics Laboratory. Salary at minimum age 21 £570 rising to £710. Qualifications G.C.E. "A" level in physics and mathematics, or similar. Work chiefly concerned with diagnosis and treatment using radioactive isotopes. Further particulars may be obtained from Hospital Secretary, Dudley Road Hospital, Birmingham, 18.

RADIATION PHYSICIST: FACULTY APpointment. Teach radiation physics, supervise radiation health programme and conduct own research. Electronic Engineer: Faculty appointment. Conduct own research and consult in biomedical problems, supervise a modern electronics shop.—Professor Charles D. Kochakian, Coordinator Research University of Alabama Medical Center, Birmingham 3, Alabama.

THE MEDICAL RESEARCH COUNCIL requires a Research Assistant with a good honours degree in biochemistry to study the factors influencing the renal excretion of calcium in man. The appointment is for three years in the first instance, and opportunities are available to register for a higher degree. Starting salary within the range £750 to £850 per annum.—Applications, with names of two referees, to Dr. A. Hodgkinson, Metabolic Disturbances in Surgery Research Unit, The General Infirmary, Leeds, 1.

RESEARCH BIOCHEMIST FOR EXPANDing Company near Windsor, to establish Control Laboratory for Enzymes and Biochemicals using modern I.R. and U.V. techniques. He would also be provided with all facilities for investigating new and unusual biochemicals. Publications encouraged. He should hold a University degree with two or three years' postgraduate or research experience in Biochemistry. Five-day week. Pension Scheme. Salary around £1,500.—Apply Box 967, T. G. Scott & Son, Ltd., 1 Clement's Inn London, W.C.2.

RESEARCH ASSISTANT WANTED AT Stoke Mandeville Hospital to help with current research on an immunological project connected with Rheumatoid Arthritis. The person appointed would work directly with the Pathologist undertaking the research. Salary £750 to £1,000 per annum according to qualifications.—Inquiries and applications, giving details of experience and the names of two referees, to the Pathologist, Stoke Mandeville Hospital, Aylesbury, Bucks.

CHEMIST OR PHYSICIST

graduate or equivalent qualification, required for the research laboratory of a North Midlands paper mill making high grade specialities. Age about 21 to 28; previous papermaking or research experience useful but not essential.

This appointment in a steadily expanding department offers interesting opportunities to a man of wide interests yet practical outlook; it carries a good salary and other benefits.

Applications, giving full details, which will be treated in confidence, should be addressed to Personnel Director, Brittains Limited, Cheddleton Paper Mills, Leek, Staffs.

AUSTRALIA

THE UNIVERSITY OF NEW SOUTH WALES
SENIOR LECTURERS OR LECTURERS
SCHOOL OF BIOLOGICAL SCIENCES

The University of New South Wales invites applications for appointment to the positions of Senior Lecturers or Lecturers in Botany in the School of Biological Sciences. The successful applicants will be expected to teach to graduate level and supervise postgraduate research activities, as well as give some assistance with elementary botanical training. Applicants should have a sound training in botany, some postgraduate research experience, and at least the following academic qualifications: Senior Lecturers: A higher degree or equivalent qualifications. Lecturers: A degree with honours or equivalent qualifications. The Botany Department is rapidly developing and the University will be interested to hear from applicants with special knowledge of any of the following fields: Cytogenetics, physiology, morphology of plant groups, angiosperm systematics or ecology. Salary: Senior Lecturer, £A.2,592 range £A.3,042 per annum. Lecturer, £A.1,772 range £A.2,477 per annum. Commencing salary is determined by qualifications and experience. First-class ship fares to Sydney of appointees and their families will be paid. After passing a medical examination, the successful applicants are eligible to join the State Superannuation Scheme. Information about the University and conditions of appointment may be obtained from the Agent-General for New South Wales in London.

Four copies of applications (including the names of two referees), should be lodged with the Agent-General for New South Wales, 56-57 Strand, London, W.C.2, and a copy forwarded by airmail to the Appointments Section, the University of New South Wales, Box 1, Post Office, Kensington, N.S.W., to arrive before July 7, 1961. Applicants outside the United Kingdom and Eire need only submit one copy of their application to the London address in addition to that sent to Sydney.

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS

Graduate, experienced in agricultural research to assist Head of Field Experiments section. Appointment in grade Scientific Officer (£717 to £1,222) or Senior Scientific Officer (£1,302 to £1,654) according to experience. F.S.S.U.

Applications, naming two referees, to Secretary by June 24. Fuller details of post on request.

BEDFORD COLLEGE

(UNIVERSITY OF LONDON)
REGENT'S PARK, LONDON, N.W.1

The Council invites applications for a Lectureship or Assistant Lectureship in Physiology. Vacant October 1, 1961; open to men and women. Initial salary according to qualifications and experience. Closing date for applications June 30, 1961.

Full particulars from the Secretary.

DEPARTMENT OF AGRICULTURE

UNIVERSITY COLLEGE OF NORTH WALES
BANGOR

Applications are invited for the post of Assistant Lecturer in the Department of Agriculture. Candidates should have an honours degree or its equivalent, with a special knowledge of crop and grassland production. The salary scale is £800 by £50 to £950 per annum and in addition there are F.S.S.U. benefits and family allowances. The appointment will date from not later than October 1, 1961.

Two copies of the application, together with the names of three referees, should reach the Registrar, from whom further particulars may be obtained, by June 17, 1961.

THE BRITISH OXYGEN COMPANY LTD have a vacancy in the Information Section of their Scientific Division for a graduate in science or engineering. The work includes abstracting and literature searching, and covers a wide range of subjects.—Applicants should write to the Administration Manager, The British Oxygen Company Limited, Scientific Division, Deer Park Road, London, S.W.19.

MEDICAL RESEARCH COUNCIL HAVE A vacancy at their Otological Research Unit, National Hospital, Queen Square, W.C.1, for a Technician, aged about 25, for Histological, Photographic and Animal experimental work. A.I.M.L.T. or equivalent qualification desirable. Salary according to age and experience, on scale £710 to £870 per annum, plus London weighting. N.H.S. superannuation.—Apply in writing to Dr. C. S. Hallpike, F.R.S., Director.

UNIVERSITY OF LONDON
KING'S COLLEGE

The College will require from October 1, 1961, an Assistant Lecturer in the Geology Department to teach Mineralogy and encourage research in this field. Salary scale: £800 by £50 per annum to £950. A London allowance of £60, family allowances, and F.S.S.U. benefits will also be payable.

Conditions of appointment and application forms may be obtained from the Registrar, King's College London, Strand, W.C.2.; completed forms must reach him by June 16.

UNIVERSITY COLLEGE OF SWANSEA

DEPARTMENT OF GEOLOGY

Applications are invited for the following posts: Research Demonstrator. Applicants should be graduates in Geology and will be expected to engage in research. Salary £700 per annum, together with F.S.S.U. benefits and family allowances. Research Assistant. Applicants should be graduates in geology or chemistry or should graduate this year. The person appointed will assist the Professor in a study of the structure and composition of fossil and recent shells. Salary in the range £500 to £650 per annum.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies), must be received not later than Saturday, June 17, 1961.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited for the post of Senior Lecturer/Lecturer in Mathematics. Applicants should be qualified in applied mathematics. The appointment will start from October 1, 1961, or as soon thereafter as can be arranged. The salary which will be not less than £1,550 per annum, will be in the scale £1,650 by £75 to £2,325 (Senior Lecturers), £1,050 by £50 to £1,400 by £75 to £1,850 (Lecturers), with F.S.S.U. and children's allowances.

Applications should reach the Registrar, the College, Keele, Staffs, from whom further particulars and application forms may be obtained, not later than June 17, 1961.

INSTITUTE OF CANCER RESEARCH: Royal Cancer Hospital. Applications are invited from B.Sc. graduates for appointment as Research Assistant in the Department of Experimental Pathology, Chester Beatty Research Institute, Fulham Road, S.W.3. The work involves the development and use of biological tests for carcinogenic and anticarcinogenic activity, and includes studies on the mechanism of carcinogenesis. The successful applicant will be expected to work for a higher degree. Initial salary in range £750 to £950 per annum with membership of F.S.S.U. and family allowances.

Apply, with names of two referees, to the Secretary, 33 Sumner Place, S.W.7, quoting ref.: 300/G/10.

MICROBIOLOGIST REQUIRED PREFERably with some research experience. Physical Chemist required for studies of trace products derived from fermentation and determined by gas chromatography. Salaries paid will be according to age and qualifications. Non-contributory pension scheme.—Apply to the Manager, the Distillers Company Limited, Glenochil Research Station, Menstries, Clackmannanshire, Scotland.

BIOCHEMISTS: B.SC. OR PH.D. REQUIRED for work on the mechanism of androgen action in protein and nucleic acid synthesis. Opportunity for advancement. Graduate work permitted for B.Sc. appointee.—Professor Charles D. Kochakian, University of Alabama Medical Center, Birmingham 3, Alabama.

GLASS-MINDED ENGINEER REquired with commercial knowledge. Able to follow projects in Chemical and Pharmaceutical Industries. Permanent and progressive position.—Applicants should submit details of education and career to date to Box 966, T. G. Scott & Son, Ltd., 1 Clement's Inn, London, W.C.2.

ST. MARY'S HOSPITAL

PADDINGTON, W.2

Senior Technician or Technician required for work in the Isotopes and Physics Department. Experience of Electronics an advantage. Whitley Council salary and conditions of service.

Applications, giving full details of age and qualifications, to Alan Powditch, House Governor.

UNIVERSITY COLLEGE OF NORTH STAFFORDSHIRE

Applications are invited from Demonstrators, and for a Curator, in the Department of Geology, tenable from September 1, 1961. Remuneration for both types of post £620 per annum.

Applications should reach the Registrar, the College, Keele, Staffs, from whom application forms and further particulars may be obtained, not later than June 30, 1961.

A WELL QUALIFIED GRADUATE (MALE) is needed immediately to take charge of the Agricultural Section of a rapidly expanding research organization in Huntingdon. A superannuation scheme is in operation. Salary according to age, qualifications and experience.—Applications, in confidence, to the Administrative Officer, Nutritional Research Unit, Huntingdon. Telephone Huntingdon 1122.

MEDICAL RESEARCH COUNCIL, CLINical Research Wing, Royal National Orthopaedic Hospital. Applications are invited for the post of Research Assistant in a research group mainly studying clinical neurophysiology. Medical qualification and some experience in electrophysiology preferred but not essential. Superannuation provided under N.H.S. Child allowance. Salary according to age and experience.—Apply in writing to the above address, Brockley Hill, Stanmore, Middlesex.

LECTURES AND COURSES

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF CHEMISTRY

A course of 20 postgraduate lectures on "Biochemistry" (to be arranged in four groups) will be given by Dr. M. W. Neil and Dr. B. R. Rabin on Mondays, 7.15 to 8.30 p.m., during the period October 2, 1961, to March 19, 1962. The course (as in previous years) is designed for students who possess a knowledge of Chemistry to degree standard. Fee: £2 for whole course or 10s. for each group.

A leaflet giving details is obtainable from the Secretary.

COUNTY OF ESSEX EDUCATION COMMITTEE

SOUTH-EAST ESSEX TECHNICAL COLLEGE
LONGBRIDGE ROAD, DAGENHAM

The next intake of students to the four-year Sandwich course preparing for Parts I and II of the Graduateship Examination of the Royal Institute of Chemistry is now being enrolled. The course will commence on September 18, 1961.

Further particulars and application forms may be obtained from the Head of the Chemistry and Biology Department at the College.

BATTERSEA COLLEGE OF TECHNOLOGY

LONDON, S.W.11
PHYSICS DEPARTMENT
(i) POSTGRADUATE COURSES

The following postgraduate courses will be held during the session 1961-62. Autumn term begins October 2, 1961.

1. Microwave Physics (full-time or part-time) leading to the M.Sc. or the Postgraduate Diploma of the College.

2. Principles and Practice of Radiation Protection (full-time or part-time) leading to the Postgraduate Diploma of the College.

3. Radiological Protection (evening course) leading to the Certificate of the College.

The Department of Scientific and Industrial Research has accepted the full-time courses in Microwave Physics and in Principles and Practice of Radiation Protection as suitable for tenure of its Advanced Course Studentships.

The two courses on radiation protection are in accordance with the recommendations of the Veale Committee Report on "Training in Radiological Health and Safety."

Full details and enrolment forms from the Secretary (Microwave Courses) or (Radiological Courses) as appropriate.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF CHEMISTRY

An evening course of Lectures and Practical Work on

THE CHEMISTRY AND MICROSCOPY OF FOOD, DRUGS AND WATER

will be given September, 1961, to July, 1962.
Lecturer in Charge: R. G. Minor, F.P.S., F.R.I.C.

The course is based on the Syllabus of the Examination for the Diploma of the Royal Institute of Chemistry. Primarily intended for those taking this examination, it is also suitable for other chemists and pharmacists who have an interest in the analysis of food and drugs. It includes Analysis and Microscopy of Food, Drugs and Water, Toxicological Analysis, Acts and Regulations relating to Food, Drugs and Poisons.

Mr. Minor will attend on Thursday, September 21, 1961, 6 to 8 p.m., to advise students.

Full particulars can be obtained on application to the Secretary.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF CHEMISTRY
COLLEGE DIPLOMA IN BIOCHEMISTRY

A two-year part-time course (Tuesdays, 2–9 p.m.) comprising lectures and laboratory work, in preparation for the above Diploma, will commence September, 1961. The entry requirement is a knowledge of Chemistry up to degree level. Students not engaged on work of an investigatory nature will be required to complete a third year devoted to a project so as to qualify for the Diploma.

Further details may be obtained from the Head of Department, to whom applications should be sent as soon as possible. Fee £3 7s. 6d. per year.

SIR JOHN CASS COLLEGE

RADIOCHEMISTRY

In October, 1961, a full-time one-year course will commence for a limited number of graduates, or persons of equivalent standing, in the principles and practice of radiochemistry. The course, which has been approved by the Department of Scientific and Industrial Research for the award of Advanced Studentships, will lead to the College Diploma, and, with suitably qualified students, will be, in part, preparation for the M.Sc. and Ph.D. degrees of the University of London.

Applications should be received as soon as possible by the Secretary, Sir John Cass College, Jewry Street, London, E.C.3.

THE FIFTH OLIVER BIRD LECTURE entitled "The Biological Control of Conception" will be given by Dr. A. S. Parkes, on June 20, 1961, at 5 p.m. in the Large Lecture Theatre, London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1. The Chair will be taken by Sir Russell Brain, Bt., D.M., F.R.C.P.—Open without fee or ticket to all interested.

GRANTS & SCHOLARSHIPS

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DEPARTMENT OF CHEMICAL ENGINEERING

Applications are invited for a Distillers Company Research Studentship, value £450 per annum, plus fees, for works leading to a higher degree on the kinetics of the gaseous oxidation of aromatic hydrocarbons.

Replies to the Secretary at the above address.

UNIVERSITY OF ABERDEEN

LAFARGE ALUMINOUS CEMENT RESEARCH FELLOWSHIP

A Junior Research Fellowship is offered in the Department of Chemistry for work on calcium aluminates and related compounds. The Fellowship is for three years, and the annual stipend will be within the range £350 to £400 (tax-free). It is expected that the work should lead to the Ph.D. degree. Applicants (men or women) should have a good honours degree in chemistry, geology or physics, or equivalent qualifications such as A.R.I.C.

Applications, giving the names of three referees, should be lodged with Professor G. M. Burnett, Department of Chemistry, Old Aberdeen, not later than June 24, 1961.

UNIVERSITY OF LONDON KING'S COLLEGE

TUTORIAL STUDENTSHIPS

are offered from October 1, 1961, in the Departments of Biochemistry, Pharmacology and Physics. The value is £425 a year, with free tuition in King's College. Maximum tenure four years. Applicants must be graduates or about to graduate, and will be required to read for a higher degree and to give a limited amount of assistance by demonstrating.

Particulars and forms from the Registrar, King's College, Strand, W.C.2, whom completed applications should reach not later than June 19.

RESEARCH GRANT

PHYSICIST or PHYSICAL CHEMIST

will be considered for a research award involving three years research at a University to work for a Ph.D. degree. The work will be on the application of electron microscopy to the study of the surface properties of silicones. It will be carried out under the direction of the University with all that implies in the way of freedom to publish.

The research grant is being made by Albright and Wilson Ltd., but the grant will be made through the University, and the successful applicant will enjoy the privileges of a research student.

The amount of the award will depend on the age and experience of the candidate. It might be given to a fresh graduate (1961 graduates will be considered) or to a more senior man for postdoctorate research. Candidates should possess a good honours degree and must be able to produce a recommendation from the Head of their own University Department, indicating a suitability for continued research in the broad field described.

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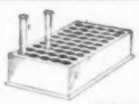
Application form and copies of the regulations may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1, to whom completed forms should be returned by July 1, 1961.



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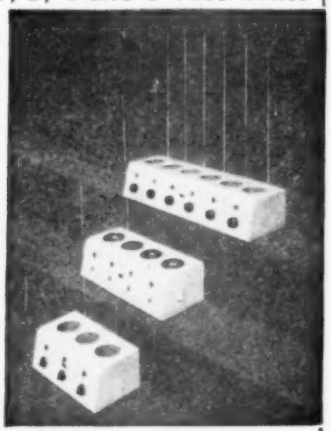

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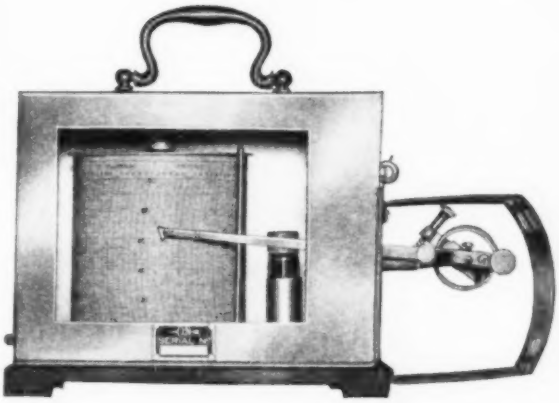

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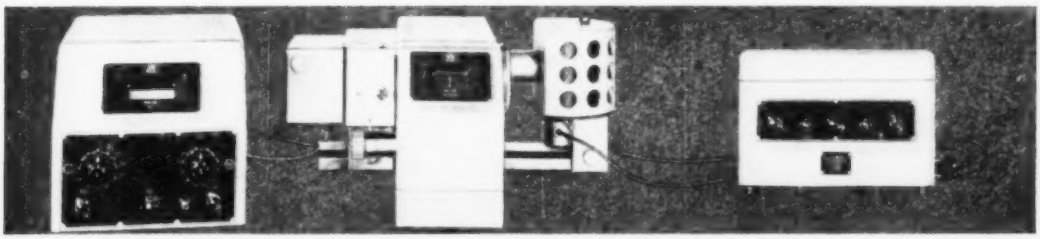

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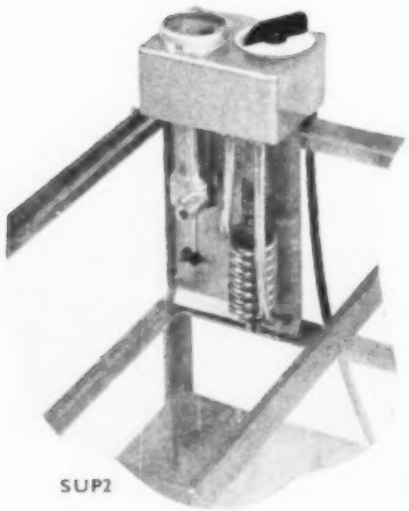

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